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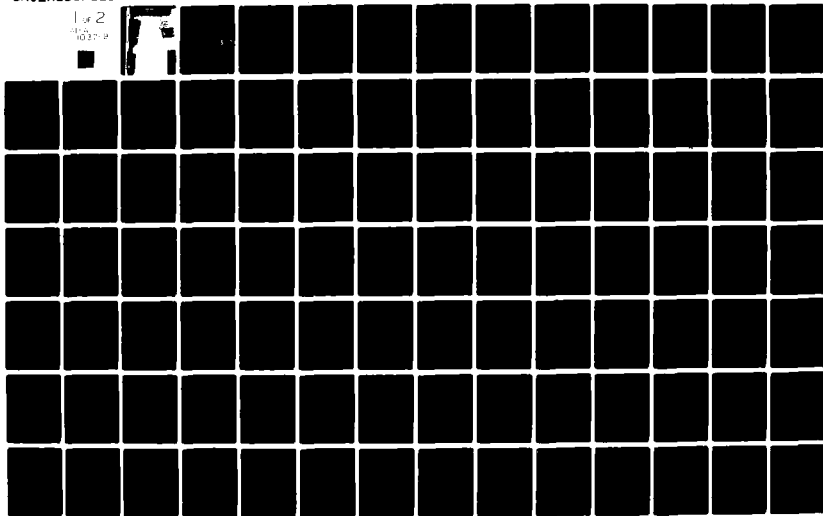
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# ANNUAL PROGRESS REPORT

CLINICAL INVESTIGATION PROGRAM  
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1 October 1980

DEPARTMENT OF CLINICAL INVESTIGATION  
TRIPLER ARMY MEDICAL CENTER  
Tripler AMC, Hawaii 96859

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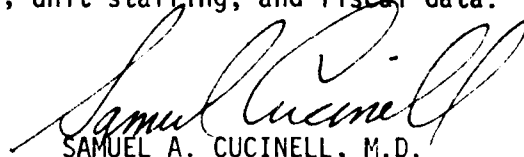
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## FOREWORD

Contained herein are progress reports on research projects fostered by the Clinical Investigation Program at Tripler Army Medical Center (TAMC) during Fiscal Year 1980.

The Clinical Investigation and Human Use Committees reviewed all proposals for their scientific merit, medical applicability, and risk to human subjects. In conducting the research described in this report, the investigators adhered to the "Guide for Laboratory Animal Facilities and Care" as promulgated by the National Academy of Sciences/National Research Council, the criteria established by the American Association for Accreditation of Laboratory Animal Care, and the principles embodied in the Declaration of Helsinki.

This Annual Progress Report contains publications, presentations, awards, proposals, preliminary findings, unit staffing, and fiscal data.



SAMUEL A. CUCINELL, M.D.

Colonel, MC

Chief, Dept of Clinical Investigation

DEPARTMENT OF CLINICAL INVESTIGATION  
TRIPLER ARMY MEDICAL CENTER

UNIT SUMMARY

A. OBJECTIVES. Providing the opportunity for professional development by scientific inquiry to the entire patient care staff is the goal of the Department of Clinical Investigation. Professional development requires that the whole process of scientific study be completed. The investigator starts with an idea or observation, completes a literature search, and designs a study. Experimentation requires support and technical assistance. The accumulated data must be organized, collated, and written in an appropriate form. The final product, in order to be meaningful both to the investigator and to medicine, must now be published.

Success in completing a scientific study is a measure of professional development. Few tyros at research succeed without help. The Department of Clinical Investigation is the mechanism for this help. The main barriers at Tripler at present are time and motivation. Since residency is time-consuming and there is no immediate benefit to the individual from scientific investigation, few wish to assume the extra burden. Incentives in addition to "professional development" will have to be found if clinical investigation at the medical center level is to reach its full potential.

B. TECHNICAL APPROACH. All research, investigations, and training activities within the Department of Clinical Investigation are conducted under the guidance of AR 40-7, AR 40-38, AR 70-25, AR 70-18, and HSC Regulation 40-23. Careful monitoring of all approved protocols is conducted in order to assure strict compliance with the applicable regulations.

C. STAFFING.

<u>Name</u>	<u>Rank</u>	<u>MOS</u>	<u>Title</u>
Cucinell, Samuel A.	COL	61F00	Chief
Goodwin, Bradford S. Jr.	MAJ	64A00	Lab Animal Veterinarian
O'Brien, John C. Jr.	CPT	68C00	Biochemist
Dotson, Carroll R.	CPT	68A00	Microbiologist
Falin, James P. Jr.	SFC	92B40	Med Lab Sp
Lewis, Clifford D.	SP5	01H20	Biomed Science NCO
Baylor, Ralph A. Jr.	SP5	91T20	Animal Sp
Conley, Lourdes M.	SP5	92B20	Med Lab Sp
Davis, Cynthia R.	SP5	91T20	Animal Sp
Ticse, Alexander	SP4	91T10	Animal Sp
Claybaugh, John R.	GS14	00413	Research Physiologist
Bryant, Gordon H.	GS11	00802	Biomedical Engineer
Toyama, Patricia S.	GS07	00301	Microbiologist
Sato, Aileen K.	GS07	00404	Biological Lab Tech
Masunaga, Lois E.	GS06	00301	Admin Tech
Cornette, Kuuleialoha	GS05	00413	Career Intern Physiologist

#### D. FUNDING

Type	Preceding Year	Current Year
Civilian personnel to include benefits	\$161,288.63	\$151,461.22
Consumable supplies	90,833.80	78,986.15
Civilian contracts to include consultants	7,633.05	3,047.30
TDY	24,419.90	16,180.58
Publications	554.75	1,622.86
Noninvestment equipment (Minor MEDCASE)	213.25	651.40
Trans & Taxes	1,019.33	409.21
Other OMA Rentals	6,813.96	7,586.80
OMA Total	292,776.67	259,945.52
MEDCASE	56,797.00	41,370.41
Other		
Military	208,569.46	220,998.58
TOTAL	\$558,143.13	\$522,314.51

E. PROGRESS. Ninety projects are reported, of which 22 have been terminated, 16 completed, and 52 are ongoing. There have been 32 publications, 8 resulting from research projects, and 38 presentations at national and regional scientific meetings, 4 resulting from research projects. The detail sheets should be examined for specific information on the individual projects.

F. PROBLEMS. The loss of authorization of two 91T animal specialists will cause difficulty in maintaining the expected level of animal research and decreased activity is to be expected.

Annual reviews of all human research by the Human Use Committee will place additional burden on the administrative office of the Department of Clinical Investigation. This office is already at the breaking point.

Deficiencies in construction in the animal colony are jeopardizing certification of these facilities.

Projects are being completed too late in the residencies to be written up by the senior investigator. For the most part, these are not being published. Ten unpublished but excellent pieces of research exist at TAMC, representing a loss of \$150,000 to the Army and embarrassment to both the investigator and Chief, Department of Clinical Investigation.

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## PUBLICATIONS

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O'Brien, J. C.: Tyrosine Aminotransferase Sensitivity to Bromodeoxyuridine During Restricted Intervals of S. Phase in Hepatoma Cells. J Cell Biol, in press. (C)

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Dotson, C. R.: Comparison of Mannitol Salt Agar/Rodac Plates to Monitor Colonization. American Society for Microbiology, Miami Beach, FL, May 1980. (C)

O'Brien, J. C. Jr.: Effect of pH, PO<sub>2</sub>, and PCO<sub>2</sub> on Lactate Consumption by Hepatocytes. Federation of American Societies for Experimental Biology, Anaheim, CA, Apr 1980. (C)

O'Brien, J. C.: The Effect of 5-Bromodeoxyuridine During S Phase on Dexamethasone Induction of Tyrosine Aminotransferase. American Society of Biological Chemists, New Orleans, LA, Jun 1980. (C)

### *DEPARTMENT OF MEDICINE*

Block, D. K.: Singultus and the Mallory-Weiss Syndrome: A Report of Two Cases. Ninth Annual William Beaumont Gastrointestinal Symposium for Federal Service Physicians, El Paso, Texas, Mar 1980.

### *DEPARTMENT OF PEDIATRICS*

Ettinger, D. D.: Head and Neck Masses in Children. American Academy of Pediatrics, San Francisco, CA, Oct 1979.

McBride, D. C.: Hyperventilation in the Treatment of Persistent Fetal Circulation. American Academy of Pediatrics Annual Meeting, San Francisco, CA, Oct 1979.

Juris, A. L.: Right Aortic Arch with Left Innominate Artery Atresia. Ninth Annual Army Cardiology Meetings, San Francisco, CA, May 1980.

### *DEPARTMENT OF SURGERY*

Andersen, C. A.: Carotid Endarterectomy at Tripler Army Medical Center. Vascular Surgery Seminar and Meeting of Military Vascular Surgeons, Washington, D.C., Dec 1979.

Andersen, C. A.: Noninvasive Diagnostic Techniques in Cerebrovascular Disease. 38th Parallel Medical Seminar, Seoul, Korea, Apr 1980.

Andersen, C. A.: Noninvasive Diagnostic Techniques in Peripheral Vascular Disease. 38th Parallel Medical Seminar, Seoul, Korea, Apr 1980.

Berrey, B. H.: Normal Findings in Arthrotomies Done for Meniscal Injuries. Annual Meeting of the Society of Military Orthopedic Surgeons, San Francisco, CA, Nov 1979.

Biggers, R. D.: The Painful Varicocele. Kimbrough Urological Seminar, Walter Reed Army Medical Center, Washington, DC, Nov 1979.

Blight, E. M., Jr.: Cancer Survival and End Result Reporting. Kimbrough Urological Seminar, Walter Reed Army Medical Center, Washington, DC, Nov 1979.

Blight, E. M., Jr.: Renal Adenoma: Therapeutic Implications. Western Section of the American Urological Association, Honolulu, HI, Mar 1980.

Collins, G. J., Jr., Rich, N. M., Andersen, C. A., and Clagett, P.: Fibromuscular Dysplasia of the Internal Carotid Artery, Management and Follow-up. National Peripheral Vascular Surgery Club, Chicago, IL, Oct 1979.

Dunn, N. P.: Total Parenteral Nutrition. American Society for Parenteral and Enteral Nutrition, Inc., Chicago, IL, Feb 1980.

Dunn, N. P.: Complications of Hyperalimentation. Gary P. Wratten Surgical Symposium, Walter Reed Army Medical Center, Washington, DC, May 1980.

Fossum, B. D.: Surgical Stone Disease in the Western Pacific. Kimbrough Urological Seminar, Walter Reed Army Medical Center, Washington, DC, Nov 1979.

Fossum, B. D.: Staghorn Calculi in Western Pacific. Western Section of the American Urological Association, Honolulu, HI, Mar 1980.

Johnson, D. R. and Reinker, K. A.: Radionuclide Scanning in the Evaluation of Retropatellar Pain. Meeting of the Society of Military Orthopedic Surgeons, San Francisco, CA, Nov 1979.

Johnson, E. A.: Hemodynamically Controlled Volume Loading in High Risk Surgical Patients. Annual Summer Scientific Meeting of the American College of Surgeons, Hawaii Chapter, Jun 80. Placed Second in Essay Contest.

Mygatt, G. G.: Spermatozoa, Zona-Free Hamster Ova and the Varicocele in the Infertile Male. Western Section of the American Urological Association, Honolulu, HI Mar 1980. (C)

Ortiz, V. N.: Use of Radioisotopes in the Early Diagnosis of Intestinal Infarction. American College of Surgeons, San Juan, Puerto Rico, Feb 1980.

Reddick, E. J.: Indications for Hyperalimentation. Gary P. Wratten Surgical Symposium, Walter Reed Army Medical Center. Washington, DC, May 1980.

Rhodes, J. R.: Evaluation of the Patient with Hypoglycemia: Report of a Case. Gary P. Wratten Medical Center, Washington, DC, May 1980.

Reinker, K. A.: Stress Fractures - A Concept in Transition. Annual Meeting, Society of Military Orthopedic Surgeons, San Francisco, CA, Nov 1979.

Rutledge, K. A.: Cutting Catheter Away from Suture Placed Through Catheter During Suprapubic Urethropexy. Western Section of the American Urological Association, Honolulu, HI, Mar 1980.

Schatz, R. E.: Technique of Hyperalimentation. Gary P. Wratten Surgical Symposium, Walter Reed Army Medical Center, Washington, DC, May 1980.

Smith, S. B.: Exploratory Laparotomy for Abdominal Trauma. 38th Parallel Medical Society, Seoul, Korea, April 1980.

Smith, S. B.: Operations for Morbid Obesity: Is There a Place for Them in Military Hospitals? Gary P. Wratten Surgical Symposium, Walter Reed Army Medical Center, Washington, DC, May 1980.

Soderdahl, D. W.: Value of Testis Biopsy in Evaluation of Male Infertility. Kimbrough Urological Seminar, Walter Reed Army Medical Center, Washington, DC, Nov 1979.

Soderdahl, D. W.: Transvesical Repair of Retrograde Ejaculation. Kimbrough Urological Seminar. Walter Reed Army Medical Center, Washington, DC, Nov 1979.

Strand, J. A.: Indications for Operation Upon the Patient with a Thyroid Nodule. Gary P. Wratten Surgical Symposium, Walter Reed Army Medical Center, Washington, DC, May 1980.

Van Sant, T. E.: Common Otolaryngic Problems, Naval Regional Medical Clinic, Kaneohe, HI, Feb 1980.

Van Sant, T. E.: Diagnosis of Early Oral Carcinoma, Hawaii County Dental Society, Hilo, HI, Aug 1980.

Van Sant, T. E. and Yim, D. W. S.: External (Combination) Rhinoplasty for the Problem Nose. American Academy of Otolaryngology, Anaheim, CA, Sep 1980.

Yim, D. W. S.: Rehabilitation of Sound Production and Speech as it Relates to Surgical Management. Laryngectomy Rehabilitation Seminar, Honolulu, HI, Feb 80.

# Detail Summary Sheet

Date: 27 Jul 81	Prot No: 138/75	Status: Ongoing
TITLE: Evaluation of the Cardioresophageal Sphincter Competence by Comparison of Intraluminal Esophageal Sphincter and Gastric Pressure with Thoracic, Hiatal, and Abdominal Pressure		
Start Date: Sep 74	Est Comp Date: Sep 82	
Principal Investigator: Gordon H. Bryant	Facility: Tripler Army Medical Center	
Dept/Sec: Dept of Clinical Investigation	Associate Investigators: Tom R. De Meester, M.D.	
Key Words: Cardioresophageal sphincter		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$3300.	Periodic Review Results: Continue

**OBJECTIVES:** To obtain comparative gastric and cardioesophageal sphincter pressures during 24-hour pH testing for nocturnal reflux.

**TECHNICAL APPROACH:** For more exact analysis of causative factors of nocturnal reflux and its surgical correction, the direct measurement of gastric and cardioesophageal pressures are to be made simultaneously with pH in 24-hour studies. Reduction of errors due to perfused side-hole catheter pressure measurements in the cardioesophageal sphincter are to be made by utilizing a three-channel, semiconductor, gastro-esophageal probe presently available. This device is to be modified so as to incorporate both a Dent sleeve system in the center section and a pH probe.

**PROGRESS:** The Dent sleeve catheter has not proved to be of advantage in 24-hour pH/esophageal pressure studies. In common with all water perfused side-hold catheter systems for intraesophageal pressure measurement, hydrostatic artifacts due to patient movement introduce uncertainties in recording interpretation. An additional research study for fabrication of a nonperfused catheter system is being instituted so as to eliminate this problem. The earlier in vitro model used in the study to define principles of lower esophageal sphincter function has been modified so as to simulate the effect on sphincter pressure of patient position. This model indicates that intraabdominal pressure and sphincter pressure is greater when the patient is lying as opposed to standing. To some extent this finding complicates the question of causative factors of nocturnal reflux.

DeMeester, TR, Wernly, JA, Bryant, GH, Little, AG, Skinner, DB: Clinical and In Vitro Analysis of Determinants of Gastroesophageal Competence: A Study of the Principles of Antireflux Surgery. Am J Surg 137:39-45, Jan 1979.

Wernly, JA, DeMeester, TR, Bryant, GH, Wang, C-I, Smith, RB and Skinner, DB: Intra-Abdominal Pressure and Manometric Data of the Distal Esophageal Sphincter. Arch Surg 115:534-539, April 1980.

### Detail Summary Sheet

Date: 28 Jul 81      Prot No: 34/79      Status: Ongoing  
 TITLE: Fabrication of a Catheter for the Determination of Liver Blood Flow in Dog and Man

Start Date: Oct 79		Est Comp Date: Sep 82
Principal Investigator: Gordon H. Bryant		Facility: Tripler Army Medical Center
Dept/Sec: Dept of Clinical Investigation		Associate Investigators: COL Samuel A. Cucinell, MC MAJ Bradford S. Goodwin, VC
Key Words: Liver blood flow		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$1250.	Periodic Review Results: Continue

**OBJECTIVES:** Development of a thermodilution catheter which will easily and repeatedly give an accurate measure of hepatic vein blood flow in larger animals.

**TECHNICAL APPROACH:** Thermistors will be removed from used Swan-Ganz catheters. Various size polyethylene or Teflon catheters will be tested for acceptability for the insertion of the thermistors. The thermistor leads will be connected to a gang of Wheatstone bridges supplied by a polygraph. The catheter will be tested in both an in vitro and in vivo system. Previous experience has demonstrated that the in vitro system is good for calibration of the system, but this rigid system does not permit the detection of the physiological variations which plague the development of new techniques. Experience with dogs will be used in the course of previously approved experiments for the evaluation of the production of lactic acid in shock.

**PROGRESS:** A single catheter containing two thermistors, so positioned in the inferior vena cava that one was above the liver at diaphragmatic level and the other below, fulfilled the purpose of this study. A single bolus of cool saline injected upstream of this device provided a pair of thermodilution curves whose area numerical difference was a direct function of hepatic venous return. By means of additional thermistors in the same catheter, renal venous flows were simultaneously obtained in a large series of flow determinations in animal studies. Developmental possibilities of the principle described are its application to arterial blood flows and the elimination of saline injection. The study on these lines continues together with potential application of the method to patients.

Bryant GH, Cucinell, SA, Goodwin BS: Hepatic Blood Flow Measurement and Blood Sampling Techniques in the Dog. To be presented at the 31st Annual Session of the American Association for Laboratory Animal Science, Indianapolis, Indiana, October 1980.



### Detail Summary Sheet

Date: 28 Jul 81      Prot No: 38/76      Status: Ongoing  
 TITLE: Further Studies on the Site of Action of Circulating Angiotensin II on Plasma ADH Concentration

Start Date: Jul 76		Est Comp Date: Sep 82
Principal Investigator: John R. Claybaugh, Ph.D.		Facility: Tripler Army Medical Center
Dept/Sec: Clinical Investigation/Physiology		Associate Investigators: CPT Clayton L. Hadick, VC
Key Words: Angiotensin Antidiuretic hormone Dog		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$3000.	Periodic Review Results: Continue

**OBJECTIVES:** To determine if circulating angiotensin II exerts its effects on stimulating ADH release via augmentation of osmotic stimulation of ADH. Studies are centered around the determination of angiotensin potentiation of osmoreceptor control of ADH of osmoreceptors located in the brain and liver.

**TECHNICAL APPROACH:** Previous approaches have included a comparison of carotid arterial and peripheral venous infusions of angiotensin II with the results clearly showing no difference in the ability of angiotensin II to stimulate ADH release. We then tied off the vertebral arteries on both sides at about C-6 and repeated the above experiments. These results were difficult to interpret because of probable reanastomosis of the vertebral blood supply. Several pilot experiments have been attempted in which we tested two hypotheses. First, since it is felt that angiotensin stimulates ADH release by potentiating osmotic stimuli, we are attempting to demonstrate a central osmotic effect on ADH release by infusing hypertonic NaCl into two exteriorized carotid arteries in conscious dogs. Alternatively, we have ligated one carotid artery, and infused into the remaining carotid artery. Having established this, we will then infuse angiotensin II either peripherally (I.V.) or via the carotid arterial circulation; thus we hope to establish whether the osmotic site and angiotensin could be the same or are, indeed, in different locations. Secondly, we are testing the angiotensin II potentiation of osmotically stimulated ADH release via stimulation of liver osmoreceptors by infusion of hyperosmotic NaCl into a chronic indwelling portal vein cannula.

**PROGRESS:** Other ongoing research had to take precedence over this project because the two coinvestigators, Dr. Goodwin and Dr. Brooks, were due to leave TAMC and both had other experiments with greater possibilities of completion within their last year. Thus, no significant progress was made on this project.

# Detail Summary Sheet

Date: 29 Jul 81	Prot No: 9/77	Status: Ongoing
TITLE: The Effect of Sodium Balance on the Vasopressin Response to Blood Volume Reduction		
Start Date: Sep 76	Est Comp Date: Sep 82	
Principal Investigator: John R. Claybaugh, Ph.D.	Facility: Tripler Army Medical Center	
Dept/Sec: Clinical Investigation/Physiology	Associate Investigators: MAJ Bradford S. Goodwin Jr., VC COL Peter J. Barcia, MC	
Key Words: Conscious dogs Blood volume reduction Sodium balance		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$1800.	Periodic Review Results: Continue

**OBJECTIVES:** To determine whether altered sodium balance increases plasma vasopressin after hemorrhage.

**TECHNICAL APPROACH:** Conscious dogs will be hemorrhaged 10% of the estimated blood volume after two weeks of low, normal, or high sodium intakes. Blood samples will be obtained prior to and five minutes after hemorrhage, and one hour after the return of hemorrhaged blood. Six dogs will be prepared with exteriorized carotid loops and with chronic indwelling left atrial cannulae. The dogs will be hemorrhaged at a rate of 0.4 ml/kg/min with blood samples taken at time 0, 10, 20, and 30 minutes, corresponding to 5, 10, and 15 percent hemorrhages. This regimen will be conducted four times on different sodium diets.

**PROGRESS:** To date we have shown that low sodium diet enhances the ADH response to equal volume hemorrhages in the same animal. This occurs despite similar initial values of plasma ADH concentration in the two states. Research by other laboratories has demonstrated a possible change in sensitivity of baroreceptor control of renin release, which may also be influencing the ADH response in a similar fashion. Inhibition of the renin-angiotensin system does not alter the ADH response to hemorrhage significantly; however, we would like to investigate this point a little further before final publication. In addition, the sensitivity of baroreceptor stimulation of ADH release in different sodium balances should be further investigated.

Claybaugh, J.R., Wade, C.E., Goodwin, B.S., and Barcia, P.J. ADH, renin, and cardiovascular responses to slow continuous hemorrhage in conscious dogs on low Na diet with inhibition of converting enzyme. Fed. Proc., 38:967, Abstract 3890, 1979.

# Detail Summary Sheet

Date: 29 Jul 81 Prot No: 14/77 Status: Completed  
 TITLE: The Role of the Renin-Angiotensin System in the Antidiuretic Hormone Response to Dehydration

Start Date: Jul 77	Est Comp Date:
Principal Investigator: John R. Claybaugh, Ph.D.	Facility: Tripler Army Medical Center
Dept/Sec: Clinical Investigation/Physiology	Associate Investigators: MAJ Bradford S. Goodwin, VC David P. Brooks, Ph.D.
Key Words: Conscious dogs Sodium depletion Angiotensin II	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost:\$2500. Periodic Review Results:

**OBJECTIVES:** These experiments are designed to determine if endogenously generated angiotensin can influence the normal release of antidiuretic hormone in response to dehydration.

**TECHNICAL APPROACH:** It has been shown in this laboratory that the renin-angiotensin system influences ADH release when dogs are dehydrated. These experiments were designed to determine if the normal response of increased ADH during dehydration is dependent upon the concomitant increased plasma renin and angiotensin. Thus, venous blood samples will be obtained before and after 48 hours of dehydration, once when the dogs are on normal sodium intake, and once after two weeks of low sodium diet.

**PROGRESS:** The effects of angiotensin-converting enzyme inhibitor (ACEI) on mean arterial blood pressure (MABP), plasma antidiuretic hormone concentration (PADH), and plasma renin activity (PRA) were studied in six conscious dogs under three conditions. In the hydrated sodium-replete condition, ACEI caused no significant changes in MABP or in PADH. In the dehydrated sodium-replete condition, ACEI caused a 9% decrease in MABP, and no change in PADH. In the dehydrated sodium-deplete condition, ACEI caused a 14% reduction in MABP and again no change in PADH. The preinfusion levels of PADH in the dehydrated states were higher ( $P < 0.01$ ) than in the hydrated state. In all protocols, ACEI caused an increase in PRA. The results indicate that the renin-angiotensin system plays a significant role in maintaining MABP in the dehydrated animal but its effect on PADH cannot be clearly determined by the experiments conducted.

Manuscript is in preparation.

# Detail Summary Sheet

Date: 27 Jul 81	Prot No: 13/79	Status: Completed
TITLE: Studies on the Occurrence of Increased Antidiuretic Hormone (ADH) Release Upon Rapid Ascent to High Altitude and the Role of Diamox in Prevention of Acute Mountain Sickness (AMS)-A Field Study at 13,800 Ft.		
Start Date: Jan 80	Est Comp Date: Sep 81	
Principal Investigator: John R. Claybaugh, Ph.D.	Facility: Tripler Army Medical Center	
Dept/Sec:	Associate Investigators:	
Clinical Investigation/Physiology	COL Samuel A. Cucinelli, MC	
Key Words:	Allen Cymerman, Ph.D.	
Acute mountain sickness	CPT John C. O'Brien, MSC	
Antidiuretic hormone	LTC David H. Gillooly, MSC	
Altitude	David P. Brooks, Ph.D.	
	CPT Rodney A. Michael, MC	
Accumulative MEDCASE Cost: \$3500	Est Accumulative OMA Cost: \$3000	Periodic Review Results:

**OBJECTIVES:** To confirm earlier observations made in studies using high altitude chambers that at some time during the first 24-hour period of exposure to high altitude there is an increased urine ADH excretion, and hopefully correlate this with increased plasma ADH concentration. The latter was not previously accomplished. We would like to see if the increased urine ADH excretion rate occurs at the same time as that in those individuals who have greatly increased urinary ADH excretion rates associated with AMS symptoms. The proposed studies should demonstrate whether or not these changes actually do occur in the "field," when many other factors such as decreased temperature, humidity, and a less confining environment will be superimposed on the effects of hypobaric hypoxia.

**TECHNICAL APPROACH:** Twelve subjects will be studied. Six will receive Diamox as a preventative for AMS symptoms and six will be untreated. The hormonal responses and water and electrolyte balance will be studied during four days prior to, and four days during exposure to an altitude of 13,800 feet. A two day post-control period will also be conducted. During the preexposure and high altitude exposure periods, two maneuvers known to affect renal handling of water and electrolytes and hormonal responses will be performed--a 16-hour dehydration and an exercise experiment. Hopefully, we will be able to detect differences in these responses between high altitude and sea level, and between the Diamox treated and untreated groups. With these differences in responses, we can perhaps find a mechanism for the ability of Diamox to ameliorate the AMS symptoms.

**PROGRESS:** Fourteen Army volunteers from various installations on Oahu (Schofield Barracks and Fort Shafter) were informed of the hazards, discomforts, and details of the experiment by verbal and movie presentation on the medical, scientific, and psychological implications of the project. Physical examinations were performed prior to the experiment and all subjects signed informed consent forms.

The experiment was conducted during August 1980 with 10 of the 14 volunteers completing all stages of the experiment. All phases of the experiment were conducted with no major technical problem. Two subjects appeared to have "classic" characteristics of moderate acute mountain sickness experiencing severe headache. They were evacuated to low altitude. Although the analyses have not been completed, some difficulty in the interpretation of the results is expected due to the severe loss of appetite by nearly all subjects. The diet, which was restricted to "Long Range Patrol Rations" supplemented with Tang and candy bars, was not acceptable by the subjects resulting in greater than expected weight losses during the study. This will probably affect certain hormonal responses, i.e., renin and aldosterone, because of the decrease in sodium intake.

We expect to present the data, in part, at the FASEB meetings in Atlanta, April 1981.

# Detail Summary Sheet

Date: 28 Jul 81	Prot No: 22/79	Status: Ongoing
TITLE: Comparison of Control of Vasopressin Release from Isolated Hypothalamoneurohypophyseal (HNS) Explants Obtained from Normal and Hypertensive Rats		
Start Date: Apr 79	Est Comp Date: Sep 82	
Principal Investigator: John R. Claybaugh, Ph.D.	Facility: Tripler Army Medical Center	
Dept/Sec: Clinical Investigation/Physiology	Associate Investigators: Kuuleialoha Cornette	
Key Words: Hypothalamoneurohypophyseal explants Hypertension		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$4,500.	Periodic Review Results: Continue

**OBJECTIVES:** Certain rat models of hypertension have elevated pituitary content, plasma concentration, and urinary excretion rates of vasopressin. The mechanism for this increased release of vasopressin is not clear and may be due to an alteration in the sensitivity of the hypothalamus to various known stimuli. By removing the hypothalamus with the stalk connection to the neurohypophysis still intact, we can eliminate many uncontrollable inputs to vasopressin release and test the sensitivity to acetylcholine, angiotensin, and osmotic stimuli, and possibly others, in order to test the hypothesis.

**TECHNICAL APPROACH:** Five-week-old, male, spontaneously hypertensive rats will be selected from the colony at the Department of Clinical Investigation, Tripler Army Medical Center, Okamoto-Aoki strain. Age-matched normotensive male control rats will be of the WKY strain. The rats will be surgically prepared with indwelling carotid arterial cannulae and placed individually into metabolism cages. Two days after surgery, daily collections of urine will be started for analysis of flow rate, urine concentrations of Na<sup>+</sup>, K<sup>+</sup> and antidiuretic hormone (ADH), and urine osmolality. Daily measurements of systolic and diastolic blood pressure will be made via the carotid arterial cannulae. After 5 days of measurements and urine collections, the rats will be sacrificed by guillotine and trunk blood collected for analysis of plasma osmolality, Na<sup>+</sup>, K<sup>+</sup> and vasopressin concentration, and plasma renin activity. The HNS will be dissected and prepared for incubation. Osmolality will be determined by vapor pressure method, Na<sup>+</sup> and K<sup>+</sup> by flame photometry. Vasopressin will be assayed by radioimmunoassay and plasma renin activity by the New England Nuclear radioimmunoassay kit. All methods are ongoing in our laboratory.

PROGRESS: The surgical skills necessary for successful dissection of the HNS preparation and the procedures involved in organ culture have been routinely performed. We have been able to demonstrate an osmotic stimulation of vasopressin from the HNS preparation in a 1-hour exposure period. Control experiments indicate a steady vasopressin production can be achieved during the necessary 5-hour block of time on the fourth day of organ culture. Changing the osmolality of the incubation medium from 290 to 315 mOsm/kg results in a significant increase in vasopressin release. Angiotensin at  $10^{-5}$  M concentration also stimulates vasopressin release in this preparation. Having established these "standard" responses, we have confidence that the preparation is responding to normal physiological stimuli.

In preliminary experiments with this preparation, we have demonstrated that aldosterone at a media concentration of 1 ng/ml will stimulate vasopressin release. The physiological significance of this finding could be far reaching, and the response is being further characterized in terms of dose and confirmation in whole animal experiments.

Difficulties in maintaining colonies of the hypertensive and normotensive control rats have hindered progress in assessing these models; however, much progress has been made on the preparation itself which was necessary before these studies could be performed.

# Detail Summary Sheet

Date: 28 Jul 81 Prot No: 6/80 Status: Completed  
 TITLE: Effect of Aldosterone on Plasma Vasopressin Concentration

Start Date: Feb 80	Est Comp Date:
Principal Investigator: John R. Claybaugh, Ph.D.	Facility: Tripler Army Medical Center
Dept/Sec: Clinical Investigation/Physiology	Associate Investigators: David P. Brooks, Ph.D.
Key Words: Aldosterone Vasopressin	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$3000. Periodic Review Results:

**OBJECTIVES:** To determine if aldosterone had any effects on plasma vasopressin concentration, plasma renin activity, or mean arterial blood pressure, the primary hypothesis being that aldosterone would stimulate vasopressin release.

**TECHNICAL APPROACH:** Aldosterone or vehicle was infused intravenously into seven conscious dogs in states of normal hydration or after 48 hours of dehydration. Aldosterone was infused at a rate of 1.6 ng/kg/min achieving plasma concentrations of 0.3 or 1.1 ng/ml respectively. These levels represent high and very high plasma levels of aldosterone, but within possible physiological ranges, i.e., not necessarily pathological. Aldosterone, renin, and vasopressin were measured using radioimmunoassay procedures that are ongoing in the Physiology Service of Department of Clinical Investigation. Mean arterial pressure was monitored continuously via a cannula inserted into the carotid artery which had previously been exteriorized in a loop of skin.

**PROGRESS:** Dehydration increased the mean osmolality, plasma renin activity (PRA), and the plasma vasopressin concentration (PADH). When the dogs were dehydrated, aldosterone infusion (16 ng kg<sup>-1</sup> min<sup>-1</sup>) was associated with statistically significant falls in mean arterial blood pressure (MABP) and PADH ( $\Delta$  = -32%; P<0.05). No change in either MABP or ADH was observed when either the same dose of aldosterone was infused into hydrated dogs or a lower dose of steroid (1.6 ng kg<sup>-1</sup> min<sup>-1</sup>) was infused into dehydrated dogs, or when vehicle was infused into both hydrated and dehydrated animals. Plasma renin activity fell to a



similar degree throughout all the experiments conducted. It is concluded that in the dehydrated animal aldosterone can cause a fall in MABP by a mechanism as yet undetermined.

Brooks, D.P. and Claybaugh, J.R. Reduced Mean Arterial Blood Pressure (MABP) and Plasma ADH after Aldosterone Infusion into Dehydrated Conscious Dogs. *Physiologist* 23:13, 1980 (Abstract 69)

Manuscript in preparation.

### Detail Summary Sheet

Date: 29 Jul 81      Prot No: 25/80      Status: Ongoing  
 TITLE: Urinary Metabolites of Vasopressin: Consequences in Radio-immunoassay

Start Date: Aug 80		Est Comp Date: Sep 82
Principal Investigator: John R. Claybaugh, Ph.D.		Facility: Tripler Army Medical Center
Dept/Sec: Clinical Investigation/Physiology		Associate Investigators: David P. Brooks, Ph.D.
Key Words: Vasopressin		Aileen Sato Kuuleialoha Cornette MAJ John C. O'Brien, MSC
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$2000.	Periodic Review Results: Continue

**OBJECTIVES:** To determine if a biologically inactive but immunologically detectable metabolite constitutes a significant amount of the vasopressin molecule excreted in the urine.

**TECHNICAL APPROACH:** Vasopressin has been shown to be metabolized in the renal nephron of some animals. Also, the values, reported for the amount of vasopressin excreted in normal man varies greatly from one laboratory to the other. We have addressed the question as to whether the former results in the latter.

Therefore, we have analyzed identical urine specimens from humans, dogs, rats, and pigs with two antisera which we have characterized as being specific to the "tail" or "ring" portion of the vasopressin molecule.

If an immunological difference is determined, we will proceed in order to find out if a chemical difference is detectable. Thus, urine will be fractionated by various methods, including sephadex, electrophoresis, high pressure liquid chromatography (HPLC), ion exchange, ultrafiltration, and others. If two chemical identities can be shown that have immunological activity with one antibody but not the other, our results would clarify the need to use a specific type of vasopressin antibody to properly measure urinary vasopressin. Our hypothesis is that this is the case, and that a "ring" directed antibody detects more of the filtered vasopressin than a "tail" directed antibody and is therefore essential for the most accurate assessment of urinary vasopressin excretion.

PROGRESS: Human, pig, rat, and dog urine contain immunologically detectable vasopressin that can be measured by both "tail" and "ring" directed antibodies, although in all species except the dog the amount measured by the "ring" directed antisera is about twofold greater than that detected by the "tail" directed antibodies.

Although syphadex, ion exchange, ultrafiltration, and proper electrophoresis have produced fractions of vasopressin that still yield immunologically different amounts of vasopressin, we have only obtained suggestive data that there are indeed two different chemical entities (possibly more) by electrophoresis. Future studies will employ HPLC.

# Detail Summary Sheet

Date: 29 Jul 81 Prot No: 6/79 Status: Ongoing  
 TITLE: Clinical Significance of Antidiuretic Hormone Levels in Disorders  
 of Fluid and Electrolyte Metabolism

Start Date: Jun 80	Est Comp Date: Sep 85
Principal Investigator: COL Samuel A. Cucinell, MC	Facility: Tripler Army Medical Center
Dept/Sec: Clinical Investigation	Associate Investigators: John R. Claybaugh, Ph.D.
Key Words: Antidiuretic hormone	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$4000. Periodic Review Results: Continue

OBJECTIVES: As a continuing part of our investigation into the influence of the antidiuretic hormone (ADH) in human metabolism, we wish to determine what influence this hormone has in a variety of clinical states.

TECHNICAL APPROACH: The main technical alteration in this protocol is that we are not doing plasma volumes in conjunction with the ADH levels. In patients with secondary hyperaldosteronism syndrome, the total blood volume is not a meaningful estimation of the state of total body hydration.

PROGRESS: Analysis of patients with hypertension show an orthostatic response of vasopressin. Patients with gastrointestinal bleeding show no increase in vasopressin. Some patients who have survived cardiac arrest have a transient diabetes insipidus.

# Detail Summary Sheet

Date: 29 Jul 81	Prot No: 26/79	Status: Ongoing
TITLE: Determination of Liver Blood Flow and Improved Technique for Sampling Hepatic Vein Blood		
Start Date: Jul 79	Est Comp Date: Sep 82	
Principal Investigator: COL Samuel A. Cucinell, MC	Facility: Tripler Army Medical Center	
Dept/Sec: Clinical Investigation	Associate Investigators: Gordon H. Bryant	
Key Words: Liver blood flow		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$5000.	Periodic Review Results: Continue

**OBJECTIVE:** To determine liver blood flow and to develop an improved technique for sampling hepatic vein blood.

**TECHNICAL APPROACH:** Methods now available for the determination of hepatic blood flow are either invasive or based on indirect chemical clearances. None of these methods is satisfactory for the accurate noninvasive quantitation of liver blood flow necessary for our continued studies into the lactic acid metabolism by the liver. It should be possible to place a thermistor catheter in the vena cava (VC) at the level of the renal and hepatic veins. Blood flow at these points might be determined by thermodilution. Hepatic vein blood flow could be estimated by subtraction of the blood flow in the vena cava at the level of the renal veins from the vena cava blood flow at the level of the diaphragm. This should be liver blood flow. It should be possible to sample pure hepatic vein blood by inflation of a balloon-equipped, double lumen catheter at the level just above the renal veins. This should cut off blood coming from the renal veins and below from entering the vena cava in the area of the hepatic veins. Blood samples from just above the balloon should be hepatic vein blood.

**PROGRESS:** The improved sampling technique studies have been completed and submitted for publication. At present, efforts are being made to obtain a manufacturer willing to fabricate a blood flow catheter for routine use.

# Detail Summary Sheet

Date: 29 Jul 81      Prot No: 28/79      Status: Ongoing  
 TITLE: Mechanism of Action and Antidote for Tricyclic Antidepressants

Start Date: Jul 79	Est Comp Date: Sep 82
Principal Investigator: COL Samuel A. Cucinell, MC	Facility: Tripler Army Medical Center
Dept/Sec: Clinical Investigation	Associate Investigators: LTC Harry M. Thomas, MC Bert Lum, Ph.D.
Key Words: Tricyclic antidepressants	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$200.      Periodic Review Results: Continue

**OBJECTIVES:** It is the intent of this study to try to define more precisely the cardiovascular toxicity of the tricyclic antidepressants (TCA) and to suggest the most rational antidote for the cardiotoxicity.

**TECHNICAL APPROACH:** A preliminary review of all cases of TCA overdose at Tripler Army Medical Center will be made to determine the cardiovascular pattern which may be peculiar to these patients in this area. A correlation with other cardioactive compounds the patient may have taken will be made. An animal model of cardiotoxicity of the TCA will be developed in the dog and rabbit. The animal will be sedated with the TCA itself. Recordings of the EKG, electrolytes, and blood gases will be made. Doses of TCA will be given to produce EKG toxicity. In some animals it will be necessary to allow the complete cardiotoxicity to evolve in order to determine the pattern of conduction abnormality leading to cardiac arrest. Once this pattern is defined, antidotes and mechanisms of altering the EKG pattern will be made. It is anticipated that a drug so rich in autonomic actions would have a cardiac effect which would operate through the autonomic nervous system. Blockade of this system at known points, i.e., ganglionic blockade, cholinergic receptor blockade, adrenergic transmitter and receptors blockade, as well as autonomic stimulants at the same levels, should alter the pharmacological pattern of TCA. If the TCA proves resistant to these manipulations, a direct quinidine-like action may exist and direct pacing may be of value.

**PROGRESS:** Studies are being carried out at the University of Hawaii on rabbits. No ventricular fibrillation has been observed.

# Detail Summary Sheet

Date: 12 Aug 81	Prot No: 30/78	Status: Terminated
TITLE: Evaluation of Three Rapid Diagnostic Methods for the Identification of <u>Hemophilus influenzae</u> in Comparison to Standard Microbiological Procedures		
Start Date: May 78	Est Comp Date:	
Principal Investigator:	Facility:	
CPT Carroll R. Dotson	Tripler Army Medical Center	
Dept/Sec:	Associate Investigators:	
Clinical Investigation/Microbiology	MAJ Charles G. Jackson, MC	
Key Words:	Raul Rudoy, M.D.	
<u>Hemophilus influenzae</u>		
Accumulative MEDCASE Cost: \$12,000.	Est Accumulative OMA Cost: \$1250.	Periodic Review Results: Terminate

**OBJECTIVES:** To determine the magnitude of diagnostic correlation between typical culture, serological, and microscopic techniques for the identification of clinical isolates of H. influenzae and immunological methods (counterimmunoelectrophoresis  $\pm$  CIE1, latex particle agglutination, and Staphylococcus-A agglutination slide tests).

**TECHNICAL APPROACH:** Cerebrospinal fluid (CSF), serum, urine, and sputum specimens from clinical cases of suspected H. influenzae at Tripler and other Oahu hospitals will be prepared for testing. On some occasions, these specimens may be stored at -70°F and tested as a group at a later date. The principal source will be bacterial meningitis presentations in pediatric patients. Additionally, similar specimens from aseptic meningitis, bacterial meningitis other than Hemophilus, and inflammations of noninfectious nature will be examined by the same techniques to establish specificity.

When possible or necessary, fluid specimens will be concentrated by standard physical and biochemical techniques. Nonspecific (positive) reactions will be eliminated by pretreating the specimen as needed; i.e., heating CSF to 100°C for 15 minutes for latex agglutination tests. The tests will be performed to detect the bacterial antigen in the body fluids. Purification and modification of the antisera, parameters of testing and specimens will be performed as needed. In particular, increased sensitivity of these reactions is expected with immunochemical purification of the antisera used.

The principal tests will be CIE, latex particle agglutination and Staphylococcus-A coagglutination, and other determinations may be made by immuno-electrophoresis, various immunological gel diffusion reactions, and ELISA. These results will be compared to that of the clinical bacteriology laboratory and to the patient's medical course.

Antisera will be prepared to the representative bacterial organisms and to the dominant surface antigen of H. influenzae type B (HITB). This antigen has been shown to be polyribose phosphate (PRP). It can be purified and used to quantitate the amount of HITB antigen in the specimen. Sterile body fluids similar to those provided by the patients will be "seeded" with known members of H. influenza type B organisms and the limits of bacterial cell detection quantitated.

PROGRESS: Early in FY 80 mission priorities required diversion of the research microbiology resources to other projects. Subsequent to work being deferred, the laboratory's staff decreased significantly, three principal investigators left the island, and commercial products for rapid diagnosis of Hemophilus influenzae were developed and marketed. The project provided extensive support to the Dept of Pediatrics but was terminated for the above reasons.



# Detail Summary Sheet

Date: 12 Aug 81 Prot No: 27/79 Status: Terminated  
 TITLE: Isolation of a Pyrogenic Exotoxin from Staphylococcus aureus

Start Date: Jun 79	Est Comp Date:
Principal Investigator: CPT Carroll R. Dotson, MSC	Facility: Tripler Army Medical Center
Dept/Sec: Clinical Investigation/Microbiology	Associate Investigators:
Key Words: Pyrogenic exotoxins <u>Staphylococcus aureus</u>	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$1000. Periodic Review Results: Terminate

OBJECTIVES: To establish methods and procedures for production and isolation of staphylococcal pyrogenic exotoxin.

TECHNICAL APPROACH: Recent isolates of Staphylococcus aureus suspected of elaborating this exotoxin and implicated in clinical disease will be procured. Isolation of S. aureus suspected of producing pyrogenic exotoxin in local hospitals will be made. Suspected organisms will be grown in air and 5% CO<sub>2</sub> atmospheres in several media to determine if toxin production can be promoted or enhanced in in vitro conditions. Culture supernates will be tested for pyrogenic factors by the rabbit bioassay. Positive pyrogenic cell-free filtrates will then be further processed to isolate the pyrogen and characterize it biochemically.

The crude toxin-containing filtrate will be treated by one or more of the following processes: ethanol precipitation, ammonium sulfate precipitation, and column chromatography as necessary. The partially purified toxin will then be isolated by thin-layer isoelectric focusing. Bioassays for pyrogenicity and epidermolytic toxin will be performed on the crude and purified forms of the isolated factors.

PROGRESS: Several modifications of chemically defined and dialysate media were evaluated for pyrogen production. None were found to produce adequate pyrogen excretion. Further acceptable pyrogen systems could not be established. One investigator withdrew from the project due to changes in clinical requirements and deferred participation in this work for this period of time.

# Detail Summary Sheet

Date: 12 Aug 81 Prot No: 8/80 Status: Completed  
 TITLE: Hemophilus influenzae Type B Surveillance at a Day Care Center:  
 Determination of Colonization Rate

Start Date: Apr 80	Est Comp Date:
Principal Investigator: Cpt Carroll Ray Dotson, MSC	Facility: Tripler Army Medical Center
Dept/Sec: Clinical Investigation/Microbiology	Associate Investigators: COL Joseph Brown III, MC CPT L. Cohen, MC R.A. Wieke, M.D. M.E. Melish, M.D.
Key Words: <u>Hemophilus influenzae</u>	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$2000. Periodic Review Results:

**OBJECTIVE:** To determine the carrier rate of Hemophilus influenzae type B (HITB) among susceptible day care center (DCC) contacts of a child with invasive HITB disease (meningitis) at the Fort Shafter DCC. The magnitude of colonization will determine whether antimicrobial prophylaxis should be considered and recommended, and for whom.

**TECHNICAL APPROACH:** Children and staff of the day care center (DCC) were screened by deep nasopharyngeal and throat cultures to determine the carrier rate for Hemophilus influenzae type B (HITB). These swabs were streaked directly on chocolate agar containing 10 µ/ml Bacitracin (CA+B) and incubated in CO<sub>2</sub>. All Hemophilus influenzae isolates were tested further by latex particle agglutination (LPA) against only HITB antisera.

**PROGRESS:** A total of 354 cultures were taken from 90 different children (casual and regular attendees) and 11 adult staff members on three different days over a five-week period. From 354 cultures, 52 (15%) had no growth and 217 (61%) grew H. influenzae, but only 13 (3.7%) of the isolates were confirmed as HITB. Carrier rates for the children on the three successive days were 9%, 3%, and 0%, respectively. Two adult staff had positive HITB results. The results of the study demonstrated that the use of CA+B media used in conjunction with LAP testing for HITB was simple and sensitive for screening cultures for HITB. The population was too small to allow double blind antimicrobial prophylaxis or comparison of two antimicrobials. All colonized individuals were successfully treated with

rifampin resulting in the elimination of the organism from this population.

Presented at the Annual Meeting of the American Society of Microbiology, Miami, Florida, May 1980.

# Detail Summary Sheet

Date: 28 Jul 81 Prot No: 1/79 Status: Completed  
 TITLE: Amylase Excretion in Laboratory Animal Models

Start Date: Jan 79		Est Comp Date:
Principal Investigator:		Facility:
MAJ Bradford S. Goodwin, VC		Tripler Army Medical Center
Dept/Sec:		Associate Investigators:
Clinical Investigation/Veterinary Svc		
Key Words:		
Amylase secretion		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$2000.	Periodic Review Results:

**OBJECTIVES:** To determine which laboratory animal is the best model for the study of amylase excretion. To determine the laboratory animal model that responds to glucagon by increased excretion of amylase.

**TECHNICAL APPROACH:** Small laboratory animals to be studied include the mouse, rat, rabbit, and cat. Each laboratory animal species will be divided into a control group and a study group. Saline diuresis will be administered if necessary to allow adequate determination of total urine output and the levels of amylase and creatinine in urine samples. The diuresis will provide an adequate sample size from the small animal species. Food and water will be available ad libitum. Normal values of amylase and creatinine have not been reported for these laboratory animals; therefore, baseline normal values will be determined for each species. The study group of laboratory animals will receive varying doses of glucagon along with the intraperitoneal saline diuresis as administered to the controls. A correlation between the concentration of glucagon administered and the increase in amylase excretion will be made. The laboratory animal species which demonstrates the most profound increase in amylase clearance after injection of glucagon should provide an excellent laboratory animal model for the study of human pancreatitis. Large animal studies will include dogs and monkeys (sheep and pigs, if necessary). Anesthetized animals will have a continuing saline diuresis with control period followed by I.V. Glucagon (approximately 1 mg). Urine will be collected during these periods for analysis.

**PROGRESS:** We found a species specific response with primates and rabbits giving either negative or no response, while cats, dogs, and pigs gave a positive response.

The data collected to date was presented at the AALAS annual meeting in Atlanta, GA., in Sep 1979. A manuscript is in preparation.

# Detail Summary Sheet

Date: 27 Jul 80 Prot No: 11/77 Status: Ongoing  
 TITLE: Enzyme Immunoassay of Arginine Vasopressin

Start Date: Apr 77	Est Comp Date: Aug 82
Principal Investigator: CPT John C. O'Brien, MSC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Clinical Investigation	Associate Investigators: John R. Claybaugh, Ph.D.
Key Words: Enzyme immunoassay	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$2500. Periodic Review Results: Continue

**OBJECTIVES:** (a) To develop the technology for and assess the clinical and research efficacy of enzyme immunoassay methods for arginine vasopressin (AV) measurements in biological fluids in comparison with now standard radioimmunoassays; and (b) to partially automate enzyme immunoassay techniques so as to allow for greater productivity in hormone measurement by routine laboratory personnel.

**TECHNICAL APPROACH:** This study consists of two phases: (1) The validation of enzyme immunoassay for AV using hormone coupled B-galactosidase, comparing results to currently available radioimmunoassays; (2) partial automation of the enzyme immunoassay for B-galactosidase.

**PROGRESS:** Preliminary experiments were initiated in developing the enzyme assay for B-galactosidase. Work, however, stopped due to personnel shortages. All supplies are on hand and work should resume in August 1981. Principal investigator upon departure from TAMC of CPT O'Brien will be John R. Claybaugh, Ph.D.

# Detail Summary Sheet

Date: 27 Jul 81 Prot No: 42/78 Status: Completed  
 TITLE: The Effect of 5-Bromodeoxyuridine on the Tumorigenicity of  
 Hepatoma Tissue Culture Cells

Start Date: Oct 78		Est Comp Date:
Principal Investigator:		Facility:
CPT John C. O'Brien, MSC		Tripler Army Medical Center
Dept/Sec:		Associate Investigators:
Clinical Investigation/Biochemistry		
Key Words:		
5-bromodeoxyuridine		
Tissue culture cells		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$7500.	Periodic Review Results:

**OBJECTIVE:** To determine if 5-bromodeoxyuridine inhibits the tumorigenicity of hepatoma tissue culture cells.

**TECHNICAL APPROACH:** The assay of tumorigenicity in the adult host was standardized as any growth appearing 75 days after a SQ injection of  $10^6$  cells. Rats received an injection of 10 day BUdR grown HTC cells or dThd grown HTC cells. After 90 days, rats not showing any tumors were injected with a second treatment of dThd grown cells.

**PROGRESS:** Those rats which had not developed tumors from the BUdR treated HTC cells were found to not develop tumors from what should have been a 100% tumorigenic dose. In effect the rats having received the BUdR treated cells were immune to the dThd grown cells. This is in striking contrast to the rapid tumor formation seen in the athymic nude mouse, whether the cells had been grown in BUdR or not. The results are being submitted for publication.

The Effect of 5-Bromodeoxyuridine During S Phase on Dexamethasone Induction of Tyrosine Aminotransferase. Presented at Annual Meeting of Biological Chemists, New Orleans, LA, June 1980.

Tyrosine Aminotransferase Sensitivity to Bromodeoxyuridine During Restricted Intervals of S Phase in Hepatoma Cells. J Cell Biol 87:629-632, Dec 1980.

# Detail Summary Sheet

Date: 22 Jul 81      Prot No: 46/78      Status: Ongoing  
 TITLE: Lactic Metabolism in Isolated Liver Cells with Regard to Anoxia,  
 Alkalosis, and Temperature

Start Date: Nov 78	Est Comp Date: Jan 81
Principal Investigator: CPT John C. O'Brien, MSC	Facility: Tripler Army Medical Center
Dept/Sec: Clinical Investigation/Biochemistry	Associate Investigators: COL Samuel A. Cucinell, MC
Key Words: Lactic metabolism	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$4000.
	Periodic Review Results: Continue

**OBJECTIVES:** To study lactate metabolism in primary cultures of rat hepatocytes.

**TECHNICAL APPROACH:** Rat liver hepatocytes will be prepared in monolayer culture. Glycogenolysis will be studied by monitoring the evolution of glucose into the media when using cells from fed rats. Glycogenolysis will be taken as the consumption of 10  $\mu$ m lactate using cells from fasted rats. The response of these cells will be measured using insulin and glucagon as stimulants.

**PROGRESS:** Rat liver cells from fed rats were found to evolve glucose and lactate into the media at a linear rate for up to two hours. Glucagon at  $10^{-9}$  M stimulated glucose production and inhibited lactate production. Several different lots of insulin did not inhibit the glucagon induced response. Using cells from fasted rats, glucagon stimulated lactate consumption. These preliminary responses are to be further studied both under the direct influence of endotoxin and using cells from endotoxic shocked rats.

"Effect of pH, PO<sub>2</sub> and PCO<sub>2</sub> on Lactate Consumption by Hepatocytes" presented at the 64th Annual Meeting of the Federation of American Societies for Experimental Biology, Anaheim, California, April 1980.

# Detail Summary Sheet

Date: 29 Jul 81 Prot No: 29/79 Status: Ongoing  
 TITLE: The Behavioral Effects of Antihypertensive Therapy in the Elderly

Start Date: Aug 80	Est Comp Date:
Principal Investigator: LTC John E. Aoki, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Family Practice	Associate Investigators: Marvelu Peterson, R.N. MAJ David Gillooly, MSC COL Samuel A. Cucinell, MC
Key Words: Antihypertensive therapy	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$500. Periodic Review Results: Continue

OBJECTIVES: To determine if treatment with antihypertensive medications in elderly hypertensive subjects produces changes in measurable areas of behavioral performance. If behavioral changes occur, does the direction of change reflect improved or impaired function?

TECHNICAL APPROACH: Elderly hypertensive patients will be placed on an alternating regimen of active antihypertensive medications and placebos. Data on blood pressure response to the two different treatments and behavioral tests and outcomes will be collected at the end of each four-week period. The two groups of subjects will be matched as closely as possible and differ only in the order in which the treatment, active medications, or placebos are given. The behavioral outcomes are conceptualized as being directly influenced by the independent variable of medication status and indirectly by the intermediate variable, blood pressure. Blood pressure is directly influenced by the independent variable, medication status.

PROGRESS: No patients have been entered into the study as yet.



# Detail Summary Sheet

Date: 13 Jul 81 Prot No: 4/80 Status: Ongoing  
 TITLE: Evaluation of PUVA in the Treatment of Resistant Psoriasis

Start Date: Aug 80	Est Comp Date:
Principal Investigator: COL Harold L. Albert, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Medicine/Dermatology	Associate Investigators:
Key Words: Psoriasis	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$250
	Periodic Review Results: Continue

**OBJECTIVE:** To determine the potential benefits of PUVA in the treatment of psoriasis resistive to other forms of therapy.

**TECHNICAL APPROACH:** In August 1980 a clinical investigation of the efficacy of psoralen plus long wave ultra-violet light in the treatment of severe psoriasis was approved. The project was included under IND #12,941 with approval of COL Charles Lewis, BAMC, principal investigator. The protocol is essentially the same as that being used by several major study groups.

**PROGRESS:** Equipment and supplies are in place and one patient has been enrolled in the study.

# Detail Summary Sheet

Date: 6 Jul 81 Prot No: 17/79 Status: Ongoing  
TITLE:

Biodetermination of Scombroid Toxin

Start Date: 1 Jul 1979	Est Comp Date: Jul 1983
Principal Investigator: LTC Thomas I. Clements, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Medicine / Emergency Medical Svc	Associate Investigators:
Key Words: Scombroid toxin	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$500.
	Periodic Review Results: Continue

**OBJECTIVES:** To design a bioassay to determine presence of unknown toxin in fish responsible for clinical scombroid poisoning. This will be attempted by correlating known patients, fish, specimens, and suspected outbreaks.

**TECHNICAL APPROACH:** A bioassay will be developed which may utilize radioactive-tagged human serum used in rabbits. Intradermal injections of the fish extract gives a "wheal and flare" which can be measured by amount of radioactivity in the area. This is most tentative. Other possibilities would include oral ingestion in laboratory animals with modified guts to watch for histamine-type response. Whatever test we develop will be correlated with retrospective analysis of the 30 to 50 cases seen in Hawaii in the last two years. The fish specimens come from these suspected cases. In addition, the investigators have made arrangements to be notified as soon as possible about any new suspected cases.

**PROGRESS:** The project is at the same state of investigation as one year ago due to lack of investigator initiative. LTC Clements will be departing this command in July 1981 and Dr. Clayton L. Hadick will become the principal investigator.

# Detail Summary Sheet

Date: 10 Jul 81	Prot No: CHE 1092	Status: Terminated
TITLE: Etoposide (VP-16-213) Combined with Cyclophosphamide Plus Cisplatin Compared to Doxorubicin Plus Cyclophosphamide Plus Cisplatin in the Treatment of Non-Small Cell Lung Cancer		
Start Date:	Est Comp Date:	
Principal Investigator:	Facility:	
LTC Mark R. Osman, MC	Tripler Army Medical Center	
Dept/Sec:	Associate Investigators:	
Dept of Medicine/Hematology-Oncology		
Key Words:		
Cancer, lung, non-small cell		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$200.	Periodic Review Results: Terminate

**OBJECTIVE:** This study aims to compare a regimen to Etoposide plus Cyclophosphamide plus Cisplatin with another which includes Adriamycin, Cyclophosphamide plus Cisplatin in non-small cell, a type of lung cancer very resistant to all therapy.

**TECHNICAL APPROACH:** Approximately 180 patients will be studied, of which 10 are estimated to be contributed by hospitals associated with the University of Hawaii. Subjects will be patients with a histologic diagnosis and measurable metastatic disease; over 16 years of age; must not have had prior chemo or radiotherapy; and must have adequate bone marrow function. Duration will be a minimum of 4 months if tumor is progressing and a maximum of 12 months if there is no evidence of tumor. Patients will be given 2 days of treatment every 4 weeks.

**PROGRESS:** OTSG approval is pending. Principal Investigator is departing TAMC. Project is therefore terminated.

# Detail Summary Sheet

Date: 10 Jul 81		Prot No: CHE 1093		Status: Terminated	
TITLE: A Phase II Trial of Mitomycin C as Topical Therapy in Non-Invasive Bladder Cancer after Failure on Thiotepa					
Start Date:			Est Comp Date:		
Principal Investigator: LTC Mark R. Osman, MC			Facility: Tripler Army Medical Center		
Dept/Sec: Dept of Medicine/Hematology-Oncology			Associate Investigators:		
Key Words: Cancer, bladder, noninvasive					
Accumulative MEDCASE Cost:		Est Accumulative OMA Cost: \$200		Periodic Review Results: Terminate	

**OBJECTIVE:** This study is to examine the effectiveness of Mitomycin C when used in patients who have failed on Thiotepa. Such patients may be referred from elsewhere or may be patients on the Thiotepa arm of Protocol B-411 who fail to respond.

**TECHNICAL APPROACH:** Thirty evaluable patients nationwide, estimate 5 in University of Hawaii associated hospitals with stages T1S and T1 bladder cancer will be involved. They will be of any age and sex. The length of involvement will be 8 weeks of weekly instillations of drug, followed by from a minimum of 1 month to over 5 years. Frequency of (1) weekly x 8 weeks; (2) every 3 months x 2 years; (3) every 6 months x 2 years; and (4) every year thereafter.

**PROGRESS:** OTSG approval pending. Principal Investigator departing TAMC. Project is therefore terminated.

# Detail Summary Sheet

Date: 10 Jul 81 Prot No: CHE 1095 Status: Terminated  
 TITLE: Etoposide VP-16 Combined with Cyclophosphamide and Doxorubicin  
 Compared to Vincristine plus Cyclophosphamide and Doxorubicin in  
 the Treatment of Small Cell Lung Cancer

Start Date:	Est Comp Date:
Principal Investigator: LTC Mark R. Osman, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Medicine/Hematology-Oncology	Associate Investigators:
Key Words: Cancer, lung, small cell	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$200
	Periodic Review Results: Terminate

OBJECTIVE: Small cell anaplastic lung cancer ("oat cell") is the most malignant of lung cancers: most patients have wide dissemination at time of diagnosis. But, recently combination chemotherapy has begun to induce significant responses in terms of number and duration in patients. Cyclophosphamide plus Adriamycin (Doxorubicin) are a standard combination of drugs which induce remissions. This study proposes to examine the possibility that adding VP-16 or Vincristine could significantly improve the clinical outcome.

TECHNICAL APPROACH: Two hundred patients from several institutions--  
 10 postulated from hospitals associated with the University of Hawaii;  
 any sex; over age 16; with a proven diagnosis of "oat cell cancer"  
 will be treated for a minimum of 3 weeks; remitting patients until  
 relapse. Frequency will be daily for 5 days, once every 3 weeks.

PROGRESS: OTSG approval pending. Principal Investigator departing  
 TAMC. Project is therefore terminated.

# Detail Summary Sheet

Date: 10 Jul 81 Prot No: CHE 1096 Status: Terminated  
 TITLE: Comparison of Efficacy of 5-FU + MeCCNU and 5-FU + CCNU in  
 Advanced Colorectal Cancer

Start Date:	Est Comp Date:
Principal Investigator: LTC Mark R. Osman, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Medicine/Hematology-Oncology	Associate Investigators:
Key Words: Cancer, colorectal	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$200
	Periodic Review Results: Terminate

**OBJECTIVE:** Five-Fluorouracil (FU) is the standard chemotherapy for advanced colorectal cancer. When given at doses of 12 mgm/kg/day followed by 15 mgm/kg/iv/week beginning on day 21, Ansfield reported 16 responses out of 46 patients. The Mayo Clinic reported that the addition of CCNU (MeCCNU) increased the FU response rate significantly. However, little overall benefit on the survival rate or duration was observed. MeCCNU in other studies has not been shown to differ significantly from CCNU, which is a marketed drug. The present study aims to compare FU vs. FU plus MeCCNU vs. FU plus CCNU.

**TECHNICAL APPROACH:** Eighty patients from several institutions, 10 estimated in Hawaii, all ages and sexes, who have measurable, proven metastatic colorectal cancer will be involved. Patients must not have had prior chemotherapy. The duration of treatment will be: (1) minimum, 4 weeks (2) maximum, until tumor progresses. Frequency of courses of 5-FU as described above, lasting one month, during which daily visits are needed the first week, every other day the second, and weekly thereafter. MeCCNU and CCNU are given orally on the first day of FU Rx and repeated once every 2 months.

**PROGRESS:** OTSG approval pending. Principal Investigator departing TAMC. Project is therefore terminated.

# Detail Summary Sheet

Date: 10 Jul 81	Prot No: CHE 1097	Status: Terminated
TITLE: Etoposide (VP-16-213) Single Agent Chemotherapy in Small Cell Lung Cancer Patients Refractory to First Line Chemotherapy		
Start Date:	Est Comp Date:	
Principal Investigator:	Facility:	
LTC Mark R. Osman, MC	Tripler Army Medical Center	
Dept/Sec:	Associate Investigators:	
Dept of Medicine/Hematology-Oncology		
Key Words:		
Cancer, lung, small cell		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$200.	Periodic Review Results: Terminate

**OBJECTIVE:** Small cell anaplastic ("oat cell") cancer of the lung is the most rapidly progressing fatal form of lung cancer. However, in recent years, combination therapy and new agents have shown effect against this tumor. "First line" therapy now usually consists of 2 to 4 drugs given simultaneously, with an expected response rate of 75% and evidence of drug-induced increase in survival. However, following relapse while on such combinations of conventional agents, there is currently little to offer. VI-16 (Etoposide) is an investigational drug with effect against oat cell cancer which might be used in such cases.

**TECHNICAL APPROACH:** Approximately 100 patients will be entered nationally, possibly 15 from hospitals associated with the University of Hawaii. These patients may be of either sex and of 16 or more years of age. They must have a proven diagnosis and advanced measurable disease, adequate marrow function. The duration of treatment will be for at least 6 weeks in which to show a response and if a response occurs, until relapse follows. Patients will receive injections of Etoposide daily for the first 5 days of successive 3 week periods.

**PROGRESS:** OTSG approval is pending. Principal Investigator is departing TAMC. Project is therefore terminated.

# Detail Summary Sheet

Date: 10 Jul 81		Prot No: CHE 1098		Status: Terminated	
TITLE: Comparison of Thiotepa and Mitomycin C as Topical Therapy in Non-Invasive Bladder Cancer					
Start Date:			Est Comp Date:		
Principal Investigator:			Facility:		
LTC Mark R. Osman, MC			Tripler Army Medical Center		
Dept/Sec:			Associate Investigators:		
Dept of Medicine/Hematology-Oncology					
Key Words:					
Cancer, bladder, noninvasive					
Accumulative MEDCASE Cost:		Est Accumulative OMA Cost: \$200.		Periodic Review Results: Terminate	

**OBJECTIVE:** To identify which drug can eradicate more localized superficial bladder tumors with the least toxicity to the host.

**TECHNICAL APPROACH:** A total of 250 patients, estimate 10/year from University of Hawaii associated hospitals, of all ages, both sexes, with proven localized, untreated or recurrent bladder cancer will be involved. The length of involvement will be minimal: 8 weeks- if tumor shrinkage of over 50% does not occur, or if tumor regrowth appears in spite of therapy; maximum: 5 or more years for those with a good therapeutic result. Frequency would be (1) first 8-12 weeks, weekly visits (2) thereafter, every 3 months x 2 years (3) every 6 months x 2 years and (4) every 12 months thereafter until relapse.

**PROGRESS:** OTSG approval pending. Principal Investigator departing TAMC. Project is therefore terminated.



# Detail Summary Sheet

Date: 10 Jul 81	Prot No: CHE 1099	Status: Terminated
TITLE: Etoposide (VP-16-213) Combined with Cisplatin Compared to Cisplatin alone in Carcinoma of the bladder		
Start Date:	Est Comp Date:	
Principal Investigator: LTC Mark R. Osman, MC	Facility: Tripler Army Medical Center	
Dept/Sec: Dept of Medicine/Hematology-Oncology	Associate Investigators:	
Key Words: Carcinoma, bladder		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$200	Periodic Review Results: Terminate

OBJECTIVE: The purpose of this trial is to observe whether these two agents given together can improve the present dismal outlook for patients with metastatic bladder cancer over that from Cisplatin alone. Cisplatin is the marketed "standard" drug and Etoposide is investigational.

TECHNICAL APPROACH: One hundred patients nationwide will be studied. An estimated 6 can be contributed from University of Hawaii associated hospitals. These will be past their 16th birthday, not have received either agent before, have measurable disease, be of either sex, have adequate marrow, liver and renal function and have proven diagnoses. Duration of treatment will be at least one month or up to 12 months if aversion occurs.

PROGRESS: OTSG approval pending. Principal Investigator departing TAMC. Project is therefore terminated.

# Detail Summary Sheet

Date: 6 Jul 81 Prot No: 25/80 Status: Ongoing  
TITLE:

Pulmonary Function in Patients with Gastroesophageal Reflux

Start Date:	Est Comp Date:
Principal Investigator:	Facility:
MAJ Rosemary F. Rodgers, MC	Tripler Army Medical Center
Dept/Sec:	Associate Investigators:
Dept of Medicine/Pulmonary	LTC Charles C. Jones, MC
Key Words:	CPT Ellen M. Pinholt, MC
Esophageal reflux	MAJ Anna K. Chacko, MC
	MAJ George H. Underwood, MC
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$200.
	Periodic Review Results: and resubmit
	Reevaluate

**OBJECTIVE:** To determine whether there are significant abnormalities in the pulmonary function studies of nonsmoking patients diagnosed to have gastroesophageal reflux.

**TECHNICAL APPROACH:** Diagnosis of gastroesophageal reflux in nonsmoking adults will be established by: (1) clinical history (with particular attention to symptoms of reflux and pulmonary disease) and physical examination; (2) Barium esophagram; (3) gastroesophageal scintiscan according to the protocol of Fisher et al. A double-lumen tube is positioned at the lower esophageal sphincter, and the patient is positioned under a collimator of a gamma counter in the supine position. Timed counts are displayed on the console of the gamma camera and photographs are taken as desired. Data from the gamma camera are stored in and processed by a data analyzer. The radiopharmaceutical is <sup>99m</sup>Tc-sulfur colloid prepared daily. The <sup>99m</sup>Tc-sulfur colloid (100 ci) is diluted in glass beaker with 300 ml of isotonic saline and instilled into the stomach via the double-lumen nasogastric tube. Both esophageal and gastric pressures are measured as the GE pressure gradient is increased in increments of 5 to 35 mm Hg. A scintiscan is obtained at a 30-sec exposure for each pressure gradient.

Incidence of pulmonary disease in these individuals will be determined by: (1) PA and lateral chest roentgenogram; (2) spirometry with and without bronchodilator (0.5 cc Isuprel in 2 cc NS); (3) gas dilution lung volume studies; and (4) DLCO SB.

At conclusion of the clinical studies, results will be examined to determine the extent of cause and effect relationship between gastroesophageal reflux and pulmonary disability.

PROGRESS: Until the project is approved by Health Services Command, we cannot initiate the procedures. However, patients' records at Tripler Army Medical Center have been reviewed to find patients for the study. A few of these patients have been contacted. Also we are working closely with Nuclear Medicine Service to perfect the esophageal reflux scintiscan technique. This procedure is well-documented as described in the literature but has never been done formally at Tripler Army Medical Center. Experience is needed in order to perfect the technique. It is somewhat hard to find patients who have esophageal reflux and do not smoke cigarettes. Because of this, patients who have asthma may be included to determine whether they also have esophageal reflux. This would necessitate a new protocol because it is a slightly different approach. This idea is being discussed.

# Detail Summary Sheet

Date: 4 Aug 81 Prot No: 2/79 Status: Ongoing  
TITLE: Glucose Modulation of Insulin Binding

Start Date: Jan 79		Est Comp Date: Sep 82
Principal Investigator: MAJ Shiao W. Shen, MC		Facility: Tripler Army Medical Center
Dept/Sec: Dept of Medicine/Endocrine		Associate Investigators:
Key Words: Insulin binding		
Accumulative MEDCASE Cost: \$1500.	Est Accumulative OMA Cost: \$1000.	Periodic Review Results: Continue

**OBJECTIVES:** To investigate the effect of glucose concentration on insulin binding; to investigate the effect of glucose preincubation on insulin binding; and to study glucose transport under varying insulin and glucose concentrations.

**TECHNICAL APPROACH:** Epididymal fat pads are removed from male Sprague-Dawley rats. Isolated fat cells are prepared by shaking at 37° C for 60 minutes in Krebs-Ringer bicarbonate buffer containing collagenase (3 mg/ml) and albumin (40 mg/ml) by the method of Rodbell. Isolated fat cells are then suspended in a buffer containing 35 mM Tris, 120 mM NaCl, 1.2 mM Mg SO<sub>4</sub>, 2.5 mM KCl, 1% bovine serum albumin, pH 7.6, and varying concentrations of glucose in a Dubnoff metabolic shaker at 37° C for 45 minutes. At the end of incubation, cells are washed and ready to be used for either <sup>125</sup>I insulin prepared at a specific activity of 100-150  $\mu$ Ci/ $\mu$ g according to the Freycht et al. modification of the method of Hunter and Greenwood. Glucose transport studies are carried out by incubating cells with 2-deoxy-II-<sup>14</sup>C-D-glucose (specific activity 2 mCi/mM) in Krebs-Ringer bicarbonate, pH 7.4, containing bovine serum albumin (10 mg/ml) at 24° C. This assay measures the total uptake of the radio-labeled 2-deoxy-glucose and is based on the principle that while 2-deoxy-glucose is transported and phosphorylated by the same process as D-glucose, it cannot be further metabolized. Calculation of glucose transport is based on the method of Olefskey.

**PROGRESS:** The isolated fat cells have proven to be difficult to work with due to the following problems. (1) The number of fat cells cannot be reliably counted. They can only be indirectly estimated by measuring

the protein contents. (2) The variability between different fat cell preparations and different rats is great. This inherent variability overshadowed the experimental variability due to manipulations of incubations. After an unsuccessful trial with hepatocytes, it was finally decided to use cultured fibroblasts from the foreskin obtained during circumcision. This system would permit repeated studies with essentially identical cells since they would all be derived from the same cell line.

### Detail Summary Sheet

Date: 4 Aug 81      Prot No: 3/79      Status: Ongoing  
 TITLE: Free and Total Insulin Levels in Insulin-Treated Diabetics

Start Date: Feb 79		Est Comp Date: Sep 81
Principal Investigator: MAJ Shiao W. Shen, MC		Facility: Tripler Army Medical Center
Dept/Sec: Dept of Medicine/Endocrine		Associate Investigators:
Key Words: Insulin binding		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$1000.	Periodic Review Results: Continue

OBJECTIVES: To measure free and total insulin levels in insulin-treated diabetics, to characterize the insulin-binding antibodies in the patients, and to correlate the free insulin levels and the characteristics of the insulin-binding antibodies to control of diabetes.

TECHNICAL APPROACH: Patients will be classified with regard to their diabetic control on the basis of personal knowledge, examination of the clinical notes, and 24-hr urine glucose. Heparinized blood, 10 ml, will be drawn from subjects after an overnight fast and again at 4 pm for plasma glucose, insulin determinations, and characterization of insulin antibodies. Free insulin and total insulin will be extracted by a modified method of Nakagawa et al. Radioimmunoassay for free insulin and total insulin will be done by dextran-coated charcoal method. Deinsulinization is accomplished by combining one part plasma with 1.25 (V/V) 0.12N HCL and 0.5 parts dextran-coated suspension. The mixture is Vortex-mixed before adding 1.25 parts 0.12 N NaOH and centrifuging twice at 2500 rpm for 30 minutes at 30 minutes at 4°C to completely remove the charcoal particles with the adsorbed insulin. The supernatant is also used for binding assay to characterize the insulin antibodies.

PROGRESS: Free and total insulin levels have been measured in 15 diabetics and 10 normals. With some additional diabetic patients, this study should be completed and written up for publication. The findings are: (1) There is no relationship between administered insulin dosage and free insulin levels in diabetic patients, (2) insulin binding to monocytes is not correlated with bound insulin or insulin dosage, but is inversely correlated to free insulin level, and (3) the maximum binding sites of insulin antibody are inversely proportional to the ratio of free/bound insulin.

# Detail Summary Sheet

Date: 4 Aug 81 Prot No: 3/80 Status: Terminated  
 TITLE: Thallium-201 Myocardial Imaging in Detecting Right Ventricular  
 Dysfunction in Chronic Obstructive Pulmonary Disease (COPD)

Start Date:	Est Comp Date:
Principal Investigator: CPT John W. Shuck, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Medicine/Pulmonary	Associate Investigators: MAJ Anna K. Chacko, MC
Key Words: Myocardial imaging Chronic obstructive pulmonary disease	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$200.
	Periodic Review Results: Terminate

**OBJECTIVES:** Several recent reports have suggested that thallium-201 imaging of the right ventricle may be the most sensitive technique available for noninvasive detection of right ventricular hypertrophy and/or dilatation from whatever cause. This study will seek to determine the correlation between the degree of abnormal thallium-201 right ventricular imaging and the degree of pulmonary hypertension in patients with COPD.

**TECHNICAL APPROACH:** This study will seek to correlate the thallium-201 right ventricular imaging findings with the degree of pulmonary hypertension in 5 patients. All patients to be studied will be those who have had right heart catheterization for established clinical reasons. Upon finding right heart abnormalities, these persons will be invited to participate in the noninvasive thallium-201 scan procedure. Statistical correlation of the results will be based upon a regression analysis between the thallium scan parameters (ejection fraction, right ventricular size, wall thickness) and the right ventricular function as measured by the cardiac catheterization data (filling pressure, ejection fraction, wedge pressure).

**PROGRESS:** The project has been terminated because of difficulties encountered.

# Detail Summary Sheet

Date: 6 Jul 81 Prot No: 19/79 Status: Ongoing

## TITLE:

Beta Blocker Heart Attack Trial

Start Date:		Est Comp Date:	
Principal Investigator: LTC Harry M. Thomas, MC		Facility: Tripler Army Medical Center	
Dept/Sec: Dept of Medicine/Cardiology		Associate Investigators:	
Key Words: Beta blocker Propranolol Heart attack			
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost:	Periodic Review Results:	Awaiting approval

OBJECTIVES: To determine the efficacy of propranolol in decreasing the incidence of sudden death and/or recurrent myocardial infarction.

TECHNICAL APPROACH: Uncomplicated postinfarction patients are treated prospectively with placebo or Inderal to see if survival in these patients is prolonged by prophylactic therapy with a beta blocker.

PROGRESS. Awaiting OTSG approval.



# Detail Summary Sheet

Date: 6 Jul 81 Prot No: 33/79 Status: Ongoing  
 TITLE: Evaluation of Amiodirone Therapy of Cardiac Arrhythmias

Start Date:	Est Comp Date:
Principal Investigator: LTC Harry M. Thomas, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Medicine/Cardiology	Associate Investigators:
Key Words: Amiodirone Arrhythmia	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$300
	Periodic Review Results: Awaiting approval

**OBJECTIVES:** To control symptomatic cardiac arrhythmias which have not been responsive to the conventional and accepted forms of treatment or whose control is dependent on the use of a drug which has been shown to be harmful to or in other ways not tolerated by the individual.

**TECHNICAL APPROACH:** Patients with life-threatening arrhythmia refractory to standard medications will be treated with an experimental drug, Amiodirone.

**PROGRESS:** Awaiting OTSG approval.

### Detail Summary Sheet

Date: 14 Jul 81	Prot No: 35/80	Status: Ongoing
TITLE: Improved Record Keeping in the MICU/CCU by Means of Table Model Computers		

Start Date: Sep 80	Est Comp Date: Sep 82
Principal Investigator: LTC Harry M. Thomas, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Medicine/Cardiology	Associate Investigators: MAJ Klaus Gierke, MC COL Samuel A. Cucinell, MC
Key Words: Record keeping	

Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$500.	Periodic Review Results: Continue
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**OBJECTIVE:** To increase diagnostic sensitivity by modern graphic display of clinical data.

**TECHNICAL APPROACH:** The Hewlett Packard 9835A computer will be programmed to display quantitative data generated by selected patients. The displays will be graphic and organized similar to data in clinical journals and textbooks. The graphic displays will include all of the quantitative clinical data generated on the patients together with timed notations of the clinical progress of the patient (including drug therapy, invasive procedures, new diagnoses, etc.) After sufficient number of patients have been studied, a quasi-objective evaluation will be performed in which a physician not associated with the patient will review the patient's chart in the classic manner compared to review of the patient's chart in addition to the graphic displays. The physicians will list the diagnosis for each day of ICU hospitalization. Statistical analysis will be by diagnosis made by physicians doing alternate type of chart review by  $\chi^2$ .

**PROGRESS:** Computer programs have been designed for accomplishing the desired goal. It was determined that additional memory capacity for the HP-9835 is necessary to accomplish the project.

# Detail Summary Sheet

Date: 12 Aug 81 Prot No: 5/80 Status: Ongoing  
 TITLE: Comparison of Daily Versus Alternate Prednisone Therapy in  
 Pulmonary Sarcoidosis

Start Date: Mar 80		Est Comp Date:
Principal Investigator: MAJ George H. Underwood Jr., MC		Facility: Tripler Army Medical Center
Dept/Sec: Dept of Medicine/Pulmonary Disease		Associate Investigators:
Key Words: Pulmonary sarcoidosis		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$300.	Periodic Review Results: Continue

OBJECTIVES: To compare the relative efficacy of equivalent dose daily vs alternate-day Prednisone therapy in stage II sarcoidosis patients with functional impairment. Techniques of evaluation must be practical and widely applicable in clinical use.

TECHNICAL APPROACH: In order to compare the therapeutic effects and complications of alternate day Prednisone to daily Prednisone in patients with sarcoid, a six-month cooperative, alternate allocation, unblinded study has been adopted.

Both methods of Prednisone dosing are used clinically, but with only anecdotal and personal experience type data to evaluate, it is impossible to select the best treatment for this disease.

The principal investigators are at WRAMC with contributions from TAMC, UDEAMC, and WBAMC.

PROGRESS: Four TAMC patients have been entered on the study. One patient completed the 6-month treatment course. Two patients were started at TAMC but are completing the study elsewhere. (There has been one death elsewhere presumably from complication of the basic disease).

# Detail Summary Sheet

Date: 29 Jul 81		Prot No: 32/80		Status: Ongoing	
TITLE: Antibiotic Prophylaxis in Vaginal Hysterectomy: A Comparison of Different Regimens; Single Dose, Multidose and Intraoperative Irrigation with Cefamandole Nafate					
Start Date:			Est Comp Date:		
Principal Investigator:			Facility:		
CPT Thomas W. Burke, MC			Tripler Army Medical Center		
Dept/Sec:			Associate Investigators:		
Dept of Obstetrics and Gynecology			CPT Eugene G. Rudd, MC		
Key Words:					
Vaginal hysterectomy					
Accumulative MEDCASE Cost:		Est Accumulative OMA Cost: \$300.		Periodic Review Results: Awaiting approval	

OBJECTIVE: To determine the efficacy of different parenteral antibiotic regimens compared with intraoperative antibiotic irrigation in decreasing the febrile morbidity and the sequelae secondary to pelvic cellulitis following vaginal hysterectomy.

TECHNICAL APPROACH: Study proposed is a prospective blinded study designed to compared antibiotic prophylaxis, single-dose parenteral, and multi-dose parenteral in decreasing the incidence of infectious morbidity following vaginal hysterectomy.

PROGRESS: Awaiting OTSG approval.

# Detail Summary Sheet

Date: 6 Jul 81 Prot No: 40/78 Status: Ongoing  
 TITLE:

Microsurgical Anastomosis of the Rabbit Oviduct

Start Date: 1 Oct 78	Est Comp Date:
Principal Investigator: LTC David A. Kallenberger, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Obstetrics and Gynecology	Associate Investigators:
Key Words: Training Microsurgery	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$2000. Periodic Review Results: Continue

OBJECTIVES: To perfect skills and increase proficiency in microsurgical techniques.

TECHNICAL APPROACH: Bilateral ligation of the fallopian tubes with microsurgical reconstruction is performed in rabbits. The reconstruction is either bilateral or unilateral.

PROGRESS: The project continues as a training protocol. LTC Heinz Osterholzer will be principal investigator as MAJ Kallenberger will be leaving TAMC.

# Detail Summary Sheet

Date: 13 Jul 81 Prot No: 23/79 Status: Completed  
TITLE: The Mechanism of Ovulation

Start Date: Oct 79	Est Comp Date:
Principal Investigator: MAJ David A. Kallenberger, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Obstetrics and Gynecology	Associate Investigators: Gordon H. Bryant Frederick Greenwood, Ph.D. Gillian D. Bryant-Greenwood, Ph.D.
Key Words: Ovulation	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$6000.
	Periodic Review Results:

**OBJECTIVES:** (1) To clarify the role of intrafollicular enzymes and ovarian hormones, particularly relaxin, in the mechanics of ovum release from the follicle. (2) To investigate the relationship between intrafollicular pressure and relaxin. (3) To assay total collagen in follicles of different sizes and relationship to intrafollicular pressure. (4) To determine the location of relaxin by fluorescein techniques. (5) To quantitate plasma relaxin levels in prepubital sows and the effect of HCG. (6) To confirm whether isolated ovarian follicles contract spontaneously.

**TECHNICAL APPROACH:** Intrafollicular pressure and the activity of relaxin were determined at intervals during the process of ovulation.

**PROGRESS:** In a series of 39 gonadotropin-stimulated gilts, intrafollicular fluid was withdrawn for relaxin and progesterone determinations by radioimmunoassay performed collaboratively by the Department of Anatomy and Reproductive Biology of the University of Hawaii. Estimation of follicular diameter was made in all follicles selected for study. Sudan black in oil was injected in sequential, measured steps during intrafollicular pressure recording for calculation of the elasticity of the stroma and its relevance to hormone levels. Follicles of 0.9 to 1.2 cm diameter showed significantly higher relaxin levels ( $p < 0.5$ ). No follicles were found to be spontaneously contracting. Publication awaits further data analysis and examination of progesterone assays just completed.

# Detail Summary Sheet

Date: 6 Jul 81 Prot No: 18/80 Status: Ongoing

TITLE: Animal Surgery as Adjunct to Gynecology Residency Program

Start Date: 1 June 1980	Est Comp Date:
Principal Investigator: CPT David A. Kallenberger, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Obstetrics and Gynecology	Associate Investigators: COL Marshall D. Matthews, MC MAJ Bradford D. Goodwin, Jr., VC
Key Words: Training Gynecological surgery	

Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$3,500.	Periodic Review Results: Continue
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OBJECTIVES: To perfect skills and increase exposure and proficiency in gastrointestinal, genitourinary and vascular procedures.

TECHNICAL APPROACH: Dogs have end-to-end anastomosis, side-to-side anastomosis, diverting colostomies, end-to-end ureteral anastomosis, and ureteral implantation as well as retropelvic vessel dissection and node dissection.

PROGRESS: The project continues as a training protocol. COL Marshall D. Matthews will be principal investigator as MAJ Kallenberger will be leaving TAMC.

# Detail Summary Sheet

Date: 6 Jul 81 Prot No: 18/79 Status: Completed  
 TITLE: Effect of Intrauterine Irrigation with Antibiotic Solution at  
 Cesarean Section

Start Date: Jul 79	Est Comp Date:
Principal Investigator: CPT Eugene G. Rudd, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Obstetrics and Gynecology	Associate Investigators: CPT William H. Long, MC MAJ Michael B. Dillon, MC
Key Words: Intrauterine irrigation Cesarean section	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$1500.
	Periodic Review Results:

**OBJECTIVES:** To determine if intrauterine irrigation with antibiotic solution will decrease the febrile morbidity and sequelae associated with pelvic infections following cesarean section.

**TECHNICAL APPROACH:** The effectiveness of intrauterine irrigation with an antibiotic solution of cefamandole nafate in reducing the incidence of endometritis after cesarean section was studied in a prospective, double-blind fashion. Ninety patients who underwent cesarean section at Tripler Army Medical Center were divided into three equal groups. Each group received one of the following treatments at the time of operation: (1) intrauterine irrigation with the antibiotic solution, (2) irrigation with normal saline solution, or (3) no irrigation. The resulting incidences of endometritis were 0%, 26.7%, and 23.3%, respectively.

**PROGRESS:** The prophylactic use of cefamandole nafate irrigation at the time of cesarean section markedly decreased the incidence of endometritis when compared to treatment with saline irrigation or no irrigation in similar groups of patients.

Published in Am J Obstet Gynecol 138:775, 1980.



# Detail Summary Sheet

Date: 29 Jul 81 Prot No: 15/80 Status: Terminated  
 TITLE: Use of Local and Regional Bupivacaine Plus Dextran at the Time  
 of Vaginal Hysterectomy in Reducing Postoperative Pain

Start Date:	Est Comp Date:
Principal Investigator:	Facility:
CPT Eugene G. Rudd, MC	Tripler Army Medical Center
Dept/Sec:	Associate Investigators:
Dept of Obstetrics and Gynecology	
Key Words:	
Vaginal hysterectomy	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$300.
	Periodic Review Results: Terminate

OBJECTIVE: To determine if pain after vaginal hysterectomy can be reduced by infiltrating the portio vaginalis and uterosacral ligaments with bupivacaine and dextran.

TECHNICAL APPROACH: The plan was to use a double blinded study of the effect of dextran in the augmentation of local anesthetic effect in vaginal hysterectomy.

PROGRESS: OTSG approval pending. Due to the departure of the principal investigator, the project is terminated.

# Detail Summary Sheet

Date: 7 Jul 81 Prot No: 26/80 Status: Ongoing  
 TITLE: A Comparison Study of Different Concentrations of Cefamandole Nafate During Cesarean Section

Start Date:		Est Comp Date:	
Principal Investigator:		Facility:	
CPT Eugene G. Rudd, MC		Tripler Army Medical Center	
Dept/Sec:		Associate Investigators:	
Dept of Obstetrics and Gynecology			
Key Words:			
Cefamandole nafate			
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$300.	Periodic Review Results:	Awaiting approval

OBJECTIVE: To compare the efficacy of intrauterine irrigation with cefamandole nafate versus parenterally administered cefamandole nafate during cesarean section in reducing the febrile morbidity and the incidence of endomyometritis and its resulting complications following cesarean section.

TECHNICAL APPROACH: This study was designed to compare intravenous antibiotics to intrauterine irrigation with antibiotic post-cesarean section.

PROGRESS: Awaiting OTSG approval.

# Detail Summary Sheet

Date: 4 Aug 81      Prot No: 21/77      Status: Ongoing  
 TITLE: Development of Clinical Assays

Start Date:	Est Comp Date:
Principal Investigator: LTC Peter Angritt, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Pathology	Associate Investigators: CPT Willie Frazier, MSC John R. Claybaugh, Ph.D. CPT John C. O'Brien, MSC COL Samuel A. Cucinell, MC COL James E. Hastings, MC
Key Words: Clinical assays	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$1000.      Periodic Review Results: Continue

**OBJECTIVES:** This study is designed to (a) familiarize the clinical pathology resident with the field of new and developing assay kits; (b) give him an opportunity to evaluate the various assay kits for cost, effectiveness, and technique; and (c) determine which of the kits would be of greatest service to TAMC.

**TECHNICAL APPROACH:** All new laboratory tests which become available commercially will be evaluated by sending for information from the manufacturer. A number of kits will be purchased from various manufacturers. Clinical specimens will be obtained from patients with established diagnoses as well as from appropriate controls. Each kit will be compared for accuracy, sensitivity, ease of performance, cost, shelf life, etc. The investigator will estimate, based on current and future hospital requirements, which test (if any) is best.

**PROGRESS:** The Abbott Laboratories A antigen and B core antigen were evaluated and found to successfully identify patients with known hepatitis A, B, and controls.

# Detail Summary Sheet

Date: 4 Aug 81 Prot No: 44/78 Status: Completed  
 TITLE: Amylase Excretion with Exercise

Start Date: Jan 79	Est Comp Date:
Principal Investigator: MAJ William G. Kavanagh, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Pathology	Associate Investigators: COL Samuel A. Cucinell, MC CPT John C. O'Brien, MSC
Key Words: Exercise Amylase excretion	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$2000. Periodic Review Results:

**OBJECTIVES:** To determine if under conditions of controlled exercise there is a relationship between the concentration of glucagon in the serum and the clearance of amylase.

**TECHNICAL APPROACH:** This experiment will make use of military volunteer marathon runners, male and female. Control (resting) levels of chemical and physiological measures will be obtained. The subjects will then run at least 20 miles. At intervals of five miles, specimens of blood and urine will be obtained, as well as physiological measures. A correlation of the plasma glucagon, which should increase continuously during the exercise, and amylase excretion will be made. No other change in the routine of marathon running will be made. Water, food, and additional stops will be made ad lib. A maximum of 12 subjects will be studied. It is best for logistical purposes, as well as competitive performance, to do the study at a practice marathon rather than the real competition, although studies at the conclusion of a true competitive marathon may yield maximal changes.

**PROGRESS:** Amylase excretion was studied in marathon runners and in runners doing 20 miles per day for 14 days (run 2, rest 1). There was a lack of correlation in marathoners before and immediately after running.

Long-term runners showed a decreased amylase excretion during rest days compared to running days.

It is clear that glucagon has a complex relationship to amylase excretion. An animal model was therefore developed to show the relation of glucagon to amylase excretion. Excretion increased in the dog and cat; no change was seen in the monkey; and in the rabbit and rat, amylase excretion decreased after glucagon administration.

A manuscript has been submitted for publication.

### Detail Summary Sheet

Date: 4 Aug 81      Prot No: 41/78      Status: Terminated  
 TITLE: Role of Complement and Antibodies in Protection Against Neonatal  
 Group B Streptococcal Infection

Start Date: Jun 79	Est Comp Date:
Principal Investigator: MAJ Charles G. Jackson, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Pediatrics/Immunology	Associate Investigators: CPT Carroll R. Dotson, MSC MAJ David K. Ohashi, MSC
Key Words: Streptococcal infection	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$1033.      Periodic Review Results: Terminate

OBJECTIVES: To evaluate the integrity of the classical and alternative pathways of complement and the presence of type specific antibodies in mothers and neonates in relation to colonization and infection with group B beta hemolytic streptococci.

TECHNICAL APPROACH: Serum from maternal-infant pairs where the infant is infected and/or colonized with GBS will be obtained in two ways. The first is retrospective, i.e., recognized by finding an infected or colonized infant in the nursery. The second method is prospective starting with maternal GBS carriers recognized during pregnancy. Since the carrier rate for GBS is roughly 25% with sensitive bacteriologic techniques, and since the incidence of GBS infection in infants is only about 3 per 1,000 live births, the prospective approach will yield primarily colonized maternal-infant pairs with only a small chance of identifying infected infants in advance.

PROGRESS: Investigator failed to complete annual report. Project terminated.

# Detail Summary Sheet

Date: 12 Aug 81 Prot No: 23/80 Status: Terminated  
 TITLE: Immunization of a Patient, Antok Dribo, with Bacteriophage  
 ØX 174

Start Date: Aug 80	Est Comp Date:
Principal Investigator: CPT Charles G. Jackson, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Pediatrics/Immunology	Associate Investigators:
Key Words: Immunization Bacteriophage ØX 174	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$1000. Periodic Review Results: Terminate

OBJECTIVES: (1) To characterize the antibody response in terms of anamnestic response and IgM to IgG switch in hyper-IgE syndrome in order to contribute to the understanding of hormonal mechanisms of this condition. (2) To better understand the degree of immunologic impairment, thus the risk of subsequent infections, in this individual patient.

TECHNICAL APPROACH: A 14-month-old Marshallese male who has hyper-IgE syndrome will be immunized with Bacteriophage ØX 174.

PROGRESS: The investigator failed to submit an annual report. The project is terminated.

# Detail Summary Sheet

Date: 29 Jul 81	Prot No: 12/80	Status: Completed
TITLE: Persistent Loop Sign in Necrotizing Enterocolitis (NEC) as an Indicator for Surgical Intervention		
Start Date: Jun 80	Est Comp Date:	
Principal Investigator:	Facility:	
MAJ Tommy Leonard, Jr., MC	Tripler Army Medical Center	
Dept/Sec:	Associate Investigators:	
Dept of Pediatrics/Neonatology		
Key Words:		
Necrotizing enterocolitis		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$400.	Periodic Review Results:

**OBJECTIVE:** To assess the predictive value of segmental bowel dilatation for surgical intervention in NEC.

**TECHNICAL APPROACH:** A retrospective analysis of records and x-rays of 21 infants treated in our Newborn Intensive Care Nursery from January 1973 to December 1978 was performed to evaluate the predictive value of a persistent segmental bowel dilatation for >24 hours to identify infants with bowel wall necrosis. Medical records were abstracted, and x-rays of the 21 study infants and 10 controls were placed in identical jackets without identifying markers. All patients were seen and treated prior to the radiologist's tenure at this institution. Twelve clinically obtained variables were compared to persistent loop for predicting necrotic bowel. These variables included weight, gestational age, duration of ventilatory support, arterial pH and pO<sub>2</sub>, and duration of umbilical artery catheterization.

**PROGRESS:** None of the control infants had a persistent loop, while 7 of 21 study infants had a persistent segmental dilatation of bowel. Four of the 7 infants expired and had necrotic bowel at surgery and/or autopsy. Three of the 7 infants with a persistent loop responded to medical management and had no clinical sequelae of NEC at follow-up evaluation. Two of the 14 infants without the sign had necrotic bowel and expired. All deaths were directly related to the necrotic bowel with perforation and sepsis. Individually or collectively, the 12 other variables were not as predictive as the persistent loop. However, by itself, persistent



loop was not a statistically significant predictor of necrotic bowel ( $r=0.447$ ,  $P>0.05$ ). The use of a persistent segmental dilatation of bowel as a criterion for surgical intervention is not warranted, but should alert the physician to the possibility of bowel wall necrosis.

Accepted for presentation at the 66th Scientific Assembly and Annual Meeting of the American Radiological Society, Dallas, November 1980.

Manuscript in preparation.

# Detail Summary Sheet

Date: 4 Aug 81 Prot No: 12/79 Status: Ongoing  
 TITLE: Intubation and Chest Tube Placement in Small Laboratory Animals

Start Date: Feb 79		Est Comp Date: Indefinite
Principal Investigator: LTC Philip G. Pettett, MC		Facility: Tripler Army Medical Center
Dept/Sec: Dept of Pediatrics/Neonatology		Associate Investigators:
Key Words: Endotracheal intubation		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$1000.	
		Periodic Review Results: Continue

**OBJECTIVES:** To provide a teaching model for medical trainees in the proper techniques of endotracheal intubation and chest tube insertion.

**TECHNICAL APPROACH:** Young kittens and rabbits housed at the Tripler Army Medical Center Animal Facility will serve as animal models. The anatomy of the thorax and airway closely approximates that of the premature human infant. Standard intubation and thoracotomy equipment will be set up on a weekly basis at a time prearranged with Clinical Investigation Service and the Newborn Medicine Service. One of the above-named investigators will accompany 1-2 junior house staff officers to the facility and provide instruction in proper technique. Each house staff officer will then use the animal models to refine his own abilities.

**PROGRESS:** Training program continues unchanged. Principal Investigator will be CPT Jose Garcia, MC, upon departure of LTC Pettett.

# Detail Summary Sheet

Date: 28 Jul 81 Prot No: 30/79 Status: Terminated  
 TITLE: Assessment of Maternal Fever in the Immediate Prenatal Period  
 as a Predictor of Perinatal Newborn Infections

Start Date:	Est Comp Date:
Principal Investigator: MAJ Leedell Reuben, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Pediatrics/Neonatology	Associate Investigators:
Key Words: Perinatal newborn infections	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$200.
	Periodic Review Results: Terminate

OBJECTIVES: To determine the incidence of serious perinatal infections in infants born to febrile mothers.

TECHNICAL APPROACH: The study population will consist of all infants born at TAMC, FAMC, and MAMC to mothers who are febrile within 24 hours prior to delivery. A control population will be determined by matching each study infant with the next infant born to an afebrile mother and matched by weight, gestational age, Apgar scores, and duration of ruptured membrane (<12 hr, 12-24 hr, >24 hr). Each study and control mother will have a blood culture and placental culture. Each study and control infant will have a peripheral blood culture, stool and umbilical cultures, CBC and platelet count, and C-reactive protein within six hours of birth. Each study infant will have a chest x-ray. A gastric aspirate for gram-stain and culture will be obtained in the delivery room or immediately on arrival to the nursery for each infant. The CBC and platelet count will be repeated at 24 hours of life. A lumbar puncture for cerebrospinal fluid evaluation will be done on those infants to be treated with antibiotics or as otherwise clinically indicated. Each infant will be treated with antibiotics according to the clinical situation at the discretion of the physician in charge of his care. If an infant is born to a mother who received antibiotics prior to the delivery and he is not started initially on antibiotics, a second blood culture will be obtained from that infant at 24 hours of life. Acute and convalescent viral titers will be obtained at birth and at 3-4 weeks, respectively, on all study and control infants. Viral cultures of nasopharynx, stool, and urine will be obtained from all infants at TAMC. The placentas of study and control infants will be examined grossly and histologically.

PROGRESS: This project was not approved by OTSG and is terminated.

# Detail Summary Sheet

Date: 28 Jul 81	Prot No: 22/80	Status: Ongoing
TITLE: Antidiuretic Hormone Secretion in the Asphyxiated Neonate		

Start Date: Aug 80	Est Comp Date: Jun 82
Principal Investigator: MAJ Leedell Reuben, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Pediatrics/Neonatology	Associate Investigators: John R. Claybaugh, Ph.D. MAJ Edwin Bollerup, MC
Key Words: Antidiuretic hormone Asphyxiated neonate	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$1000. Periodic Review Results: Continue

**OBJECTIVE:** To evaluate and determine the physiologic response of antidiuretic hormone (ADH) secretion in cerebrospinal fluid (CSF) and plasma in the newborn infant who has experienced central nervous system (CNS) injury, hypoxemia and asphyxia, i.e., is there evidence for independent control of release of ADH into the CSF and plasma. Also, we intend to test the hypothesis that hypoxemia will increase the release of ADH into the CSF and consequently lead to increased pressure in the CSF or other evidence of cerebral edema.

**TECHNICAL APPROACH:** Subjects used for this study will be neonates admitted to the Special Care Nursery for evaluation of sepsis or possible sepsis. In addition, all newborn infants with intracranial hemorrhage, CNS injuries from birth trauma, and neonates experiencing severe asphyxia with hypoxemia increased intracranial pressure and cerebral edema. Asphyxia will be defined as follows: A 5 min Apgar score  $\leq 6$  and/or arterial blood pH  $\leq 7.25$  on admission to Special Care Nursery. On admission, each patient's Apgars, temperature, heart rate, blood pressure, and weight are recorded. Arterial blood gases are required for evaluation of acidosis, hypoxemia, and oxygen requirement. From each neonate, when possible, CSF opening pressure will be recorded, then 2 ml of spinal fluid will be collected and mixed with 0.1 ml of 1.0 N HCl/ml of CSF and immediately frozen for ADH assay. In addition, 5 ml of blood will be placed in a heparinized tube and plasma preserved with 0.1 ml of 1.0 N HCl/ml and frozen for ADH assay. Plasma and CSF will also be evaluated for  $\text{Na}^+$  and  $\text{K}^+$  concentration and osmolality. The data collected will be assessed to determine the correlation of CSF ADH

and plasma ADH and the correlations of both of these parameters to known stimulators of ADH release, i.e., plasma osmolality, CSF osmolality, body temperature, and arterial blood pressure and  $\text{PaO}_2$  and  $\text{PaCO}_2$ . These data will be analyzed by multiple regression analysis to determine which factors most influence the independent release patterns of ADH into either the plasma or CSF. If computerized axial tomography scans are performed, an attempt will be made to correlate cerebral edema with high CSF ADH levels. It is anticipated that about 100 patients would provide sufficient information regarding the above-mentioned correlations.

PROGRESS: Project is ongoing and still active; initial data continues to be collected. Data to the present time is now being analyzed. To date, 22 neonates have been assessed for CSF ADH concentration, and an additional 13 neonates have been assessed for six 4-hour sequential urine samples post partem, some of whom also had CSF ADH determinations. Correlations between CSF and/or urinary ADH with  $\text{PaO}_2$ ,  $\text{PaCO}_2$ , pH, bone excess, body temperature, systolic blood pressure, and APGAR scores, are presently underway. MAJ Edwin Bollerup will become principal investigator upon the departure from TAMC of MAJ Reuben.

# Detail Summary Sheet

Date: 13 Jul 81 Prot No: 16/79 Status: Completed  
 TITLE: Childhood Psychosis and Trifluoperazine Therapy: Placebo  
 Comparison (Double-Blind Study)

Start Date:	Est Comp Date:
Principal Investigator: COL Nicholas L. Rock, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Psychiatry	Associate Investigators:
Key Words: Childhood psychosis	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$300.
	Periodic Review Results:

**OBJECTIVES:** To compare in a double-blind manner the therapeutic effects of trifluoperazine (Stelzine) in the treatment of childhood psychosis (infantile autism, childhood schizophrenia, atypical development).

**TECHNICAL APPROACH:** Children stabilized on a maintenance dose of trifluoperazine will be entered into the study which will consist of the random distribution of coded medication by the TAMC pharmacy. At least half the children at one time should be on placebo and the other half on the regular medication. Each week the rating scale will be completed by parents, special program, and TAMC staff to evaluate the level of psychotic behavior. After one month, the procedure will be reversed, in that those on placebo will be given drugs and those who have been on regular drugs will receive placebo. This procedure will proceed for the third and fourth months so that each group will have received an alternating placebo dose and therapeutic dose over the four months. After the fourth month, the code will be broken.

**PROGRESS:** Study has been completed. Results have verified effectiveness of medication in childhood psychosis. Rating scales are not much value; clinical evaluation is still legitimate; blood serum levels are not reliable.

**PUBLICATION:** Rock NL, Shearer RD, Skoberg PK: Therapeutic Dosage and Window with Trifluoperazine in Childhood Psychosis (Autism). Journal of Psychiatric Treatment and Evaluation 2:241-244, 1980.

# Detail Summary Sheet

Date: 6 Jul 81	Prot No: 14/76	Status: Ongoing
TITLE: Clinical Evaluation of Cisternography Utilizing Indium-111 DTPA		
Start Date: 2 Jan 76	Est Comp Date:	
Principal Investigator:	Facility:	
MAJ Anna A. Chacko, MC	Tripler Army Medical Center	
Dept/Sec:	Associate Investigators:	
Dept of Radiology/Nuclear Medicine		
Key Words:		
Cisternogram		
Indium-111 DTPA		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost:	Periodic Review Results: Continue

**OBJECTIVES:** Since there is currently a moratorium on the use of RISA in cisternography, it is our purpose to substitute Indium-111 DTPA for RISA in this procedure. Indium-111 DTPA (Diethylene Triamine Penta Acetic Acid) is presently in the third phase of investigation under the FDA. The agent will be used for the following: (1) Detection of communicating hydrocephalus; (2) Detection of noncommunicating hydrocephalus; (3) Aid in determining whether a cerebrospinal fluid shunt would be required; (4) Detection of rhinorrhea; and (5) Study of cerebrospinal fluid dynamics.

**TECHNICAL APPROACH:** Radionuclide cisternography will be performed utilizing Indium-111 DTPA in those patients with the above-described medical problems. Results obtained from these procedures will be compared with results obtained with earlier RISA cisternography and with results obtained by other laboratories. The results will be correlated with the results of clinical findings, by roentgenographic studies and autopsy of surgical material where available to determine the accuracy and limitations of this procedure in each of the categories of disease studied.

Approximately 0.5 mCi Indium-111 DTPA will be administered by intrathecal or intraventricular injection to patients referred to the Nuclear Medicine Laboratory for scintigraphic evaluation of cerebrospinal fluid pathways. The patients will meet the following criteria: (1) nonpregnant and over the age of 18 years unless special indications for study exist; (2) all will have either known or suspected alterations of cerebrospinal fluid flow. No subject without manifest or suspected disease will be studied.

**PROGRESS:** Cisternography was performed on 6 patients during FY 80. The study proved to be a useful adjunct in assessing the cerebrospinal fluid dynamics of all patients.

# Detail Summary Sheet

Date: 6 Jul 81	Prot No: 31/76	Status: Ongoing
TITLE: Clinical Evaluation of Fluorescent Scanning of the Thyroid with Americium-241		
Start Date: 1 Aug 76	Est Comp Date:	
Principal Investigator: MAJ Anna K. Chacko, MC	Facility: Tripler Army Medical Center	
Dept/Sec: Dept of Radiology, Nuclear Medicine Svc	Associate Investigators:	
Key Words: Fluorescent scanning Thyroid		
Accumulative MEDCASE Cost: \$30,000.	Est Accumulative OMA Cost: \$9,000.	Periodic Review Results: Continue

OBJECTIVES: To determine the value of fluorescent thyroid imaging as compared with other modalities of thyroid imaging in the diagnosis and treatment of a variety of thyroid abnormalities.

TECHNICAL APPROACH: Dual studies are intended to involve both conventional thyroid scanning and fluorescent technique scanning in patients studied in the Thyroid Clinic at TAMC.

PROGRESS: No fluorescent scans were performed during FY 80. The fluorescent scanner was inoperative due to a leak in the liquid nitrogen storage tank. Although the scanner was recently returned to service, staff shortages have made it impractical at this time to resume the project. At such time as the personnel shortages are resolved, the project will again be resumed.



# Detail Summary Sheet

Date: 6 Jul 81 Prot No: 19/80 Status: Ongoing  
 TITLE: Study of the Internal Mammary Lymph Nodes in Patients with  
 Inner Quadrant Breast Cancer

Start Date:	Est Comp Date:
Principal Investigator: MAJ Anna K. Chacko, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Radiology/Nuclear Medicine	Associate Investigators: LTC Charles F. Miller, MC LTC Mark R. Osman, MC MAJ Marilyn P.M. Ordonez, MC CPT Edward J. Faleski, MC COL Paul L. Shetler, MC MAJ Alfred J. Landry, MSC
Key Words: Breast Cancer Tc 99m antimony sulfide colloid	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$200. Periodic Awaiting Review Results: approval

OBJECTIVES: To determine if the presence or absence of pathology in internal mammary nodes will make any difference in the morbidity or mortality of patients with breast cancer.

TECHNICAL APPROACH: Patients studied will be women who have proven or highly suspected breast carcinoma. No pregnant or lactating women, or those under 18 years of age will be administered the drug, unless the benefits to be gained by the study outweigh any risks in the opinion of the physician.

The antimony sulfide colloid will be obtained from the Union Carbide Corporation. Tagging will be performed locally with Tc 99m.

Tc 99m antimony sulfide colloid, 500  $\mu$ Ci, will be injected into the posterior rectus sheath on the ipsilateral side. Two and one half to three hours later a camera will be utilized with a suitable collimator to image the internal mammary lymph nodes on the ipsilateral side.

PROGRESS: To date, approval for performing this study at TAMC has not been granted by The Surgeon General's Human Subjects Research Review Board. Therefore, no progress on this study has been made.

# Detail Summary Sheet

Date: 13 Jul 81 Prot No: 20/80 Status: Ongoing  
 TITLE: In Vivo Evaluation of Hepatobiliary System with Tc 99m HIDA

Start Date:		Est Comp Date:	
Principal Investigator:		Facility:	
MAJ Anna Chacko, MC		Tripler Army Medical Center	
Dept/Sec:		Associate Investigators:	
Dept of Radiology/Nuclear Medicine			
Key Words:			
Hepatobiliary system			
99m Tc HIDA			
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$500.	Periodic Review Results:	Awaiting approval

OBJECTIVE: To demonstrate the safety and efficacy of Tc 99m Imino-di-acetic Acid for the in vivo evaluation of hepatobiliary system in patients suspected of having hepatobiliary disease.

TECHNICAL APPROACH: The study will include patients suspected of having hepatobiliary disease which can include jaundice of any cause, abdominal pain in which cholecystitis is suspected, or suspected mass lesions of the liver from other clinical or diagnostic studies. No pregnant women, lactating women, or persons under 18 years of age will be administered the drug, unless the benefits gained outweigh the risks in the opinion of the investigator. The HIDA will be obtained in kit form from Union Carbide. Labeling will be done in the Nuclear Medicine Service by experienced personnel. The suggested dose range employed in the average (70 kg) patient is 2-15 mCi: 99 mTc depending on the level of a recent serum bilirubin determination or clinical estimate of the degree of jaundice, if no serum bilirubin level is available.

PROGRESS: Although this protocol has not been approved for routine use at TAMC by The Surgeon General's Human Subjects Research Review Board, authority for emergency use was requested and received on one occasion in the FY 80 period. Results of the procedure were most remarkable and proved to be a valuable aid in the diagnosis of hepatobiliary disease.

# Detail Summary Sheet

Date: 6 Jul 81 Prot No: 15/80 Status: Ongoing  
TITLE:

The National Study of Contrast Media Reactions

Start Date:	Est Comp Date:
Principal Investigator:	Facility:
COL Raoul O. Hagen, MC	Tripler Army Medical Center
Dept/Sec:	Associate Investigators:
Dept of Radiology	CPT Ronald L. Embry, MC
Key Words:	
Contrast media	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$200.
	Periodic Review Results: Awaiting approval

OBJECTIVE: To study the effects of premedication on the incidence of contrast media reactions.

TECHNICAL APPROACH: This is a randomized, double-blind study involving participating medical centers across the U.S.A. As many as 200,000 patients receiving IVPs may eventually be enrolled in this study. The patients will be assigned to one of four groups: (1) 32 mg of Medrol in the evening preceding urography and 32 mg of Medrol again in the morning at least 2 hours before the IVP is given. (2) 32 mg of Medrol in the morning at least 2 hours before the IVP is given. (3) Placebo in the evening preceding urography and again in the morning at least 2 hours before the IVP is given. (4) Placebo in the morning at least 2 hours before the IVP is given. The intravenous pyelogram will be carried out with the usual technique employed in each institution. Appropriate medications to treat reactions, if they occur, will be immediately available.

PROGRESS: Awaiting OTSG approval.

# Detail Summary Sheet

Date: 4 Aug 81	Prot No: 39/78	Status: Ongoing
TITLE: The Value of Gallium Scans in Determining Prosthetic Aortic Graft Infections in Canines		
Start Date: Aug 78	Est Comp Date: Sep 82	
Principal Investigator:	Facility:	
LTC Charles A. Andersen, MC	Tripler Army Medical Center	
Dept/Sec:	Associate Investigators:	
Dept of Surgery/Vascular Surgery	MAJ Anna K. Chacko, MC	
Key Words:	MAJ Bradford S. Goodwin, VC	
Aortic graft	CPT Carroll Ray Dotson, MSC	
Gallium scans		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$3000.	Periodic Review Results: Continue

OBJECTIVES: To explore the methods of diagnosing a graft infection.

TECHNICAL APPROACH: An aortic dacron graft is placed in mongrel dogs. The dogs are then placed in a control group or given a dose of IV Staphylococcal bacteria to infect the graft. After varying periods of time, the grafts are studied with Gallium scans to determine whether or not the Gallium scan can accurately predict the presence of an infected graft. After an appropriate time, the animals are sacrificed and the grafts are examined grossly and histologically and bacteriologically for evidence of a graft infection.

PROGRESS: The initial series of dogs demonstrated that Gallium could indeed predict an infected graft. However, we are lacking an adequate number of control dogs. In addition to the work with Gallium, the initial study was expanded to include CAT scan evaluation of the infected grafts. Again, it appeared that the CAT scan could very accurately predict a graft infection. However, again, adequate controls were lacking. In the next fiscal year, additional dogs need to be studied for controls of both the Gallium study and CAT scan study.

# Detail Summary Sheet

Date: 4 Aug 81 Prot No: 7/80 Status: Terminated  
 TITLE: Lower Extremity Venous Valvular Incompetence During Pregnancy

Start Date:		Est Comp Date:
Principal Investigator:		Facility:
LTC Charles A. Andersen, MC		Tripler Army Medical Center
Dept/Sec:		Associate Investigators:
Dept of Surgery/Vascular Surgery		
Key Words:		
Venous valvular incompetence		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$200.	Periodic Review Results: Terminate

**OBJECTIVE:** To determine the incidence and consequence of saphenofemoral venous incompetence during pregnancy. To determine whether saphenofemoral incompetence developing during pregnancy subsides or resolves after delivery of the fetus in some patients.

**TECHNICAL APPROACH:** Pregnant females will be followed at monthly intervals during the pregnancy with Doppler untrasound examinations of the common femoral vein and saphenofemoral junction. The degree of valvular incompetence will be measured. The examinations will be completely non-invasive and will be utilizing Doppler ultrasound which is currently in wide use in OB practice. These women will also be followed postpartum to determine whether or not the valvular incompetence is reversible.

**PROGRESS:** The study has been terminated due to a lack of personnel support to do the venous Doppler examinations.

# Detail Summary Sheet

Date: 17 Jul 81 Prot No: 11/80 Status: Ongoing

TITLE:

Audiovisual Counseling of Preoperative Patients

Start Date: Jan 80		Est Comp Date: Jul 81
Principal Investigator: LTC C.A. Andersen, MC		Facility: Tripler Army Medical Center
Dept/Sec: Dept of Surgery		Associate Investigators:
Key Words: Audiovisual counseling		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$200	
		Periodic Review Results: Continue

**OBJECTIVE:** To evaluate the effectiveness of an audiovisual tape, together with a verbatim transcript of the audio portion of the tape, in preparing patients for an operation.

**TECHNICAL APPROACH:** All patients undergoing elective cholecystectomy will be counseled by the operating surgeon utilizing the format that they have previously used. In addition to the routine counseling, 50 percent of these surgeons' (randomly selected) patients will be shown a videotape on gallbladder surgery by a nurse who is not involved in their care. These patients will then be given a printed transcript of the tape. The nurse will have all cholecystectomy patients complete a questionnaire in regard to attitudes. After each patient in the study has been discharged, the nurse will review the chart and record pertinent data. All patients will be asked to complete a retrospective questionnaire.

This study is to be conducted as a joint project with the Straub Clinic and the Kaiser Foundation. The data will be collected, compiled and stored for 12 months. At the completion of the study the data analysis will be conducted in two parts, beginning with a one-time batch key-punching of the data with a computer analysis to follow.

**PROGRESS:** The clinical work has been completed at Tripler Army Medical Center. Additional patients are being studied at Straub Clinic, Queen's Medical Center, and Kaiser Hospital. Following the completion of patient studies at the other hospitals, the data will be compiled and appropriate papers written and submitted.

# Detail Summary Sheet

Date: 4 Aug 81 Prot No: 6/77 Status: Ongoing  
TITLE: Regrowth of Small Intestinal Mucosal Surface Area

Start Date: Nov 76	Est Comp Date: Sep 82
Principal Investigator: COL Peter J. Barcia, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Surgery/General Surgery	Associate Investigators: CPT Clayton L. Hadick, VC
Key Words: Small intestinal mucosal surface Neogut	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$4182.
	Periodic Review Results: Continue

**OBJECTIVES:** To explore methods of increasing small intestinal mucosal absorptive area following massive resections, and to determine the technical feasibility and functional results of certain specific procedures.

**TECHNICAL APPROACH:** Based on previous successful studies in dogs and rats with growth of neogut on the serosal surface of the colon, the next step will be to (1) perform similar studies in the pig (which has a gastrointestinal tract and physiologic responses similar to man); and (2) attempt growth of neogut on the peritoneal surface of the abdominal wall. This would mirror the clinical circumstance if no suitable colonic recipient site were available.

Five pigs will undergo lapartomy under general anesthesia and each animal will have two grafts placed. After varying periods of time (maximum 8-12 weeks) at a second procedure, these grafts could be harvested and intestinal continuity would be restored.

**PROGRESS:** An initial series of dogs has provided us with the following data: (1) A new small intestinal mucosa will grow across the serosa of the colon under these circumstances; and (2) the graft is mechanically functional, i.e., food is propelled in a relatively normal fashion through the graft, and these animals do not develop small intestinal obstruction.

This project won second prize in the Hawaii American College of Surgeons Annual Essay Contest, Honolulu, Hawaii, June 1977. Presented to the William Beaumont Gastrointestinal Symposium, El Paso, Texas, March 1978.

### Detail Summary Sheet

Date: 17 Jul 81	Prot No: 37/76	Status: Completed
TITLE: Knee Hinged Cylinder Cast - Sprained Knee Study		

Start Date: Jul 76		Est Comp Date:
Principal Investigator: MAJ B. Hudson Berrey, MC		Facility: Tripler Army Medical Center
Dept/Sec: Dept of Surgery/Orthopedic Svc		Associate Investigators: COL Dennis J. Sullivan, MC
Key Words: Knee-hinged cylinder cast		

Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$1000.	Periodic Review Results: Terminate
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**OBJECTIVES:** To determine the feasibility of nonoperative early ambulation and physical therapy in a knee hinged cylinder cast as treatment for acute severe sprains of the knee.

**TECHNICAL APPROACH:** Patients with clinical history and physical examination compatible with sprained medial or lateral collateral ligaments of the knee will be evaluated radiographically. If the knee is deemed to be grossly unstable and may be treated operatively, he will be offered the choice between treatment in a cast brace with early ambulation and protected rehabilitation versus surgery. Those treated non-operatively will then be started on a painless, permissive progressive protected rehabilitation to deter quadriceps atrophy and apply physiologic stresses to the knee. These patients will be followed at one-month intervals up to six months and then at one year. Patients will be compared to the operated cases regarding changes in stability, range of motion, and thigh girth at the end of treatment and at six months, and function in regard to return to former activity.

**PROGRESS:** Since the conception of this project, it has become clinically apparent that the "grossly unstable" sprained knee is ideally treated by operative repair. Only when strong relative or absolute contraindications to operative treatment exist should treatment by knee hinged cylinder cast be recommended. Accordingly, for the past two years we have been unable to follow the technical approach described in the original proposal. A final report is in preparation documenting the experiences of the study.

Presented at the Annual Meeting of the Western Orthopedic Association, October 1977.



# Detail Summary Sheet

Date: 4 Aug 81 Prot No: 2/78 Status: Completed  
TITLE: Saluting with a Supracondylar Fracture

Start Date: Nov 77	Est Comp Date:
Principal Investigator: MAJ B. Hudson Berrey, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Surgery/Orthopedics	Associate Investigators: CPT Bruce W. Wulfsberg, MC COL Bruce F. LaFollette, MC
Key Words: Fracture, supracondylar	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$1500. Periodic Review Results:

**OBJECTIVES:** To assess the efficacy of positioning the forearm to control rotation of the distal fragment in a supracondylar fracture.

**TECHNICAL APPROACH:** Patients who sustain a supracondylar fracture of the humerus were carefully examined for rotary malalignment of the fracture clinically and radiographically. If reduction and skeletal traction were chosen as the method of treatment, management of rotation was attended to by positioning of forearm. The results of treatment regarding deformity of the elbow were assessed by clinical and radiographic examination.

**PROGRESS:** A paper demonstrating this traction method of treating children with supracondylar fractures was presented at the Society of Military Orthopedic Surgeons Meeting in November 1977. This technique was presented as a Scientific Exhibit at a meeting of the American Academy of Orthopedic Surgeons in February 1979. This paper was presented as a scientific paper at the Annual Meeting of the Western Orthopedic Association in October 1980.

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# Detail Summary Sheet

Date: 17 Jul 81 Prot No: 1/80 Status: Terminated  
 TITLE: Minimum Exposure Requirements for an Excretory Urogram (XU)

Start Date:	Est Comp Date:
Principal Investigator:	Facility:
COL Edward M. Blight, Jr., MC	Tripler Army Medical Center
Dept/Sec:	Associate Investigators:
Dept of Surgery/Urology	
Key Words:	
Excretory urogram	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$200. Periodic Review Results: Terminate

**OBJECTIVE:** To determine whether any films may be omitted from a routine XU without decreasing the sensitivity of the study.

**TECHNICAL APPROACH:** A urology staff member will review the KUB and 10-minute film (postvoid) of each routine XU done by the Urology Service. He must not have previously seen or heard a report of the film. This will be done each afternoon following the official Urology reading session, after the diagnosis has been entered in the x-ray book. On the basis of the two films, the urologist will either give a diagnosis or ask to see further films until a diagnosis can be made. At the end of each reading session, his reading will be compared with the official (GU) reading, any discrepancies noted, and the comparative number of films noted. In case of any missed diagnoses, a determination will be made as to whether the abnormality was diagnosable on the films viewed and just missed by the reader. After 300 studies have been thus compared, results will be studied to determine how many exposures have been avoided and the significance of any missed diagnoses.

**PROGRESS:** This project was terminated almost before it began because the radiology residents' academic interest was to get the most out of an IVP rather than to determine the least number of x-rays that could be exposed with adequate clinical information.

# Detail Summary Sheet

Date: 17 Jul 81 Prot No: 11/76 Status: Terminated

TITLE:

Subcutaneous Mastectomy

Start Date: Oct 1975		Est Comp Date:
Principal Investigator: LTC Maxwell A. Cooper, MC		Facility: Tripler Army Medical Center
Dept/Sec: Dept of Surgery/Plastic Surgery		Associate Investigators:
Key Words: Mastectomy, subcutaneous		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$950.	Periodic Review Results: Terminate

**OBJECTIVES:** To determine the efficacy and results of the procedure over a prolonged period of time for prevention of signs and symptoms of fibrocystic disease and/or mastodynia; additional objective, to decrease risk factor for breast cancer especially in high-risk patients.

**TECHNICAL APPROACH:** Maintain long-term contact with patients undergoing subcutaneous mastectomy and compare their quantity and quality of life with (a) female population at large, (b) females with benign breast diseases, and (c) females with breast malignancies. Determine risk factors from medical history and pathological specimens; compare results of conservative surgery versus radical surgery for benign, premalignant, and malignant diseases.

**PROGRESS:** The study was terminated as the number of patients who could be followed over a long period of time due to the transient military population was insignificant. The objectives have been proven by other studies and medical literature and are now considered to be standard surgical procedures.

# Detail Summary Sheet

Date: 14 Jul 81 Prot No: 25/78 Status: Ongoing

TITLE: Microvascular Training Protocol

Start Date: May 78	Est Comp Date: Indefinite
Principal Investigator: LTC Maxwell A. Cooper, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Surgery/Plastic Surgery	Associate Investigators:
Key Words: Training Microvascular	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$1450. Periodic Review Results: Continue

OBJECTIVES: To develop and maintain microvascular suture technique among the Plastic Surgery Service staff, TAMC, and to familiarize general surgery and other specialty residents with the techniques of microvascular anastomosis.

TECHNICAL APPROACH: To divide and reanastomose the common femoral artery and vein of rats. One pair of vessels per week with delayed evaluation of patency is planned. Later expansion to other models such as the rabbit ear and dog intestine and vas deferens is possible.

PROGRESS: During FY 80, the laboratory was utilized 1-2 times per week while both Plastic Surgeons were available for work at TAMC. However, with Dr. Cooper's departure in May and the excess workload, the laboratory has not been utilized as desired. Two human clinic cases, as a direct result of this expertise, have been accomplished during this period of time.

Another plastic surgeon is scheduled to arrive in July. He has some expertise in this field and plans are being made to include a wider scope of teaching, both for the Plastic Surgery staff and the residents.

# Detail Summary Sheet

Date: 29 Jul 81 Prot No: 21/79 Status: Terminated  
 TITLE: Experimental Closure of the Rat or Dog Bladder with Surgical  
 Auto-Suture, Stainless Steel Staples for Closing Bladder Defects

Start Date: May 79	Est Comp Date:
Principal Investigator: MAJ Basil D. Fossum, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Surgery/Urology	Associate Investigators: MAJ Bradford S. Goodwin, VC CPT Carroll R. Dotson, MSC
Key Words: Auto-suture Bladder	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$3000. Periodic Review Results: Terminate

OBJECTIVES: To determine feasibility and safety of using Auto-suture stainless steel staples for closing bladder defects.

TECHNICAL APPROACH: An anesthetized dog or rat undergoes incision of the lower abdomen with exposure of the bladder. The dome of the bladder is excised and the remaining bladder closed with a row of surgical staples using a model TA-55 or TA-30 suture device. The bladder is opened in periods of 3, 6, and 12 months and examined for calculi or other anatomic or microscopic defects.

PROGRESS: The bladders of ten rats and four dogs were opened and surgically closed using surgical nonabsorbable metal staples. On reexamination of the bladders of the rats, two were found to contain calculi of a composition of magnesium ammonium phosphate associated with infection and/or foreign body. To date, bladders of the dogs have not been reexamined. The study has been terminated due to the departure of the investigator.

# Detail Summary Sheet

Date: 20 Jul 81 Prot No: 27/80 Status: Ongoing  
 TITLE: Pattern of Injury in Motorcycle Accidents

Start Date: Jul 80		Est Comp Date:
Principal Investigator:		Facility:
CPT Gerald Q. Greenfield, Jr., MC		Tripler Army Medical Center
Dept/Sec:		Associate Investigators:
Dept of Surgery/Orthopedic Svc		
Key Words:		
Injuries, motorcycle		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$300.	Periodic Review Results: Continue

OBJECTIVE: To define the circumstances surrounding motorcycle-connected injuries.

TECHNICAL APPROACH: A questionnaire will be utilized to collect information on each accident victim. This will include lengths of ownership, type of motorcycle, and injury produced as well as length of any hospitalization or duty limitation.

PROGRESS: Clinical data are being gathered and collated. No conclusions have yet been reached.

# Detail Summary Sheet

Date: 20 Jul 81 Prot No: 28/80 Status: Completed  
TITLE: Rollerskating Injuries

Start Date: Aug 80	Est Comp Date:
Principal Investigator: CPT Gerald Q. Greenfield, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Surgery/Orthopedic Svc	Associate Investigators: LTC Kent A. Reinker, MC
Key Words: Injuries, rollerskating	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$1500. Periodic Review Results:

OBJECTIVE: To define the types of injuries associated with rollerskating.

TECHNICAL APPROACH: Data was collected through review of files of the Orthopedic Surgery Service. When necessary, patients were contacted by telephone to answer specific questions. Injury films were reviewed to verify the diagnoses.

PROGRESS: One hundred forty injuries due to rollerskating were studied. Most frequent were upper extremity injuries in the 6 to 15 year old group. The great majority of those injured wore no protective equipment and continue to wear none. Wrist protectors appear to be the most important item of protective equipment, especially if combined with proper falling technique.

Presented at the 1980 Annual Meeting of the Society of Military Orthopedic Surgeons, San Antonio, Texas.



# Detail Summary Sheet

Date: 20 Jul 81 Prot No: 33/80 Status: Ongoing  
 TITLE: Evaluation of Outpatients with Low Back Pain

Start Date: Sep 80	Est Comp Date: Sep 81
Principal Investigator: CPT Gerald Q. Greenfield, Jr., MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Surgery/Orthopedic Svc	Associate Investigators:
Key Words: Pain, low back	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$500. Periodic Review Results: Continue

OBJECTIVE: To define the types of patients seen in the Orthopedic Clinic with low back pain. Also studied will be the causative factors and response to therapy.

TECHNICAL APPROACH: Questionnaires will be used to collect a portion of the data. Clinical records of these patients will be reviewed. Answers to questions will be compared in an attempt to define causative factors, pain pattern, and response to therapy in the "typical" back pain patient.

PROGRESS: Data are still being accumulated and collated.

# Detail Summary Sheet

Date: 28 Jul 81 Prot No: 17/78 Status: Ongoing  
 TITLE: Human Implantation of Intraocular Lenses

Start Date: Aug 78	Est Comp Date: Indefinite
Principal Investigator: COL John J. Kearney, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Surgery/Ophthalmology	Associate Investigators:
Key Words: Intraocular lenses	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$500.
	Periodic Review Results: Continue

**OBJECTIVES:** The adjunctive study of the effects of implantation of intraocular lenses in humans and establishment of a satisfactory technique.

**TECHNICAL APPROACH:** Standard intracapsular and extracapsular techniques will be utilized, followed by insertion of Choyce style anterior chamber lenses. Additional types of intraocular lenses may be included in this study as time progresses. During this reported period only Tennant Anterior Chamber (Precision Cosmet Co.) lenses have been employed.

**PROGRESS:** At present, 12-15 lenses are implanted monthly. Some problems have been encountered. Three patients required peripheral iridectomy for aphakic pupillary block. Two patients with wound leak required resuturing. One patient had poorly controlled elevated intraocular pressure and macular edema. Two patients had retinal detachment. One patient required removal of implant because of malpositioning (a lens was not reinserted). Two patients had significant vitreous hemorrhage. As more experience is obtained, the procedure of intracapsular lens extraction and anterior chamber implantation is a safe procedure giving excellent visual results. This relates well to the experience of other investigators.

# Detail Summary Sheet

Date: 14 Jul 81 Prot No: 29/80 Status: Ongoing  
 TITLE: Radioisotope Scanning in the Diagnosis of Bone and Joint Infections

Start Date: Sep 80	Est Comp Date: Sep 81
Principal Investigator: CPT Edmund C. Landry, Jr., MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Surgery/Orthopedic Svc	Associate Investigators:
Key Words: Radioisotope scanning Infections, orthopedic	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$500. Periodic Review Results: Continue

OBJECTIVES: To evaluate the usefulness of radioisotope scanning in the early diagnosis of orthopedic infections; also, to identify situations in which radioisotope scanning should be employed early on in the diagnostic procedure.

TECHNICAL APPROACH: Orthopedic inpatient files from 1977 through 1979 will be reviewed and patients with the diagnoses of septic arthritis, diskitis, and osteomyelitis will be evaluated. X-rays and scans when performed will be analyzed in an attempt to evaluate the ultimate diagnosis as identified by clinical, radiographic, and radioisotope examinations.

PROGRESS: Clinical material is being gathered and collated.

# Detail Summary Sheet

Date: 14 Jul 81 Prot No: 31/80 Status: Ongoing  
TITLE: The Diagnosis and Treatment of Septic Arthritis

Start Date: Sep 80		Est Comp Date: Sep 81
Principal Investigator: CPT Edmund C. Landry, Jr., MC		Facility: Tripler Army Medical Center
Dept/Sec: Dept of Surgery/Orthopedic Svc		Associate Investigators:
Key Words: Arthritis, septic		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$300.	Periodic Review Results:

**OBJECTIVE:** To evaluate present diagnostic and therapeutic procedures in septic arthritis, including the identification of specific problem joints, causative organisms, and other contributing etiologic factors based upon the extensive experience at Tripler Army Medical Center.

**TECHNICAL APPROACH:** Tripler Army Medical Center inpatient files will be searched and 100 consecutive cases of septic arthritis evaluated. Evaluation will comprise the following criteria: age; joint or joints involved; presenting systemic symptoms; time to diagnosis from onset; predisposing factors; origin - whether hematogenous, post-traumatic, or postoperative; associated osteomyelitis or not; laboratory studies, including complete blood count with differential and sed rate, cultures of the joint blood and other positive cultures; aspirations performed, how many, and the white blood cell count of the joint fluid at each determination during the patient's disease course; antibiotic therapy, whether intravenous, oral, or both, and how long for each; the time from beginning treatment until the patient was clinically well; residual problems if known; and hospital bed days. Once this information has been compiled, statistical analysis will helpfully yield a composite picture of the patient with septic arthritis. This will be further carried on to analyze the bacteriologic components of the disease, the origin, and its relation to the bacteriologic organisms, the form of treatment, and its relationship to the clinical course and hospital stay, the presence or absence of associated osteomyelitis and its effect upon the clinical course, and if specific joints are more prone to delayed diagnosis, and the efficacy of various forms of treatment available for each joint. Furthermore, predisposing factors will be identified along with analysis of age groups and susceptibility. The

antibiotic regimen will also be analyzed along the line of complications from antibiotic therapy, length of time of intravenous and/or oral therapy, and its correlation with the patient's recovery. Cases in which residual deformities occurred will be specifically analyzed to determine how they differed from the remaining group in their clinical management.

PROGRESS: Clinical material is being gathered and collated.

# Detail Summary Sheet

Date: 29 Jul 81	Prot No: 14/80	Status: Ongoing
TITLE: Partial Cystectomy Followed by Cholecystectomy and Augmentation Cystoplasty with the Gallbladder in Dogs		
Start Date: Jun 80	Est Comp Date: Sep 81	
Principal Investigator: MAJ George G. Mygatt, MC	Facility: Tripler Army Medical Center	
Dept/Sec: Dept of Surgery/Urology	Associate Investigators: MAJ Bradford S. Goodwin, VC	
Key Words: Cystoplasty Bladder defects		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$3000.	Periodic Review Results: Continue

OBJECTIVE: To determine the feasibility of closing bladder defects with a free graft of gallbladder.

TECHNICAL APPROACH: Gallbladders have been used to correct surgical defects in the domes of urinary bladders in eight dogs.

PROGRESS: All dogs survived the procedure. At six months follow-up, it was impossible to grossly differentiate the suture line between the two organs. Histological studies are underway.

# Detail Summary Sheet

Date: 17 Jul 81	Prot No: 18/78	Status: Terminated
TITLE: Incidence of Injury to Recurrent Laryngeal Nerves during Thyroidectomy		
Start Date:	Est Comp Date:	
Principal Investigator: CPT Jeffrey Panosian, MC	Facility: Tripler Army Medical Center	
Dept/Sec: Dept of Surgery/General Surgery	Associate Investigators: COL John E. Major, MC	
Key Words: Thyroidectomy Laryngeal nerves		
Accumulative MEDCASE Cost: \$4308.20	Est Accumulative OMA Cost: \$250.	Periodic Review Results: Terminate

**OBJECTIVES:** Documentation of the incidence of injury to recurrent laryngeal nerves by pre and postoperative indirect laryngoscopy of all patients undergoing thyroidectomy.

**TECHNICAL APPROACH:** Preoperative indirect laryngoscopy of all patients undergoing thyroidectomy at Tripler Army Medical Center with fiberoptic laryngoscope. Postoperative indirect laryngoscopy within three days of the operation with fiberoptic laryngoscope. Follow-up examination at 7 days to 6 weeks of all patients showing evidence of nerve injury whether subclinical or associated with voice disturbances. Report incidence of nerves showing evidence of injury.

**PROGRESS:** Project terminated because of transfer of the principal investigator and associate investigator to new duty stations. No data was obtained.

# Detail Summary Sheet

Date: 20 Jul 81 Prot No: 14/79 Status: Ongoing  
TITLE: Retropatellar Pain Syndrome

Start Date: June 1979	Est Comp Date:
Principal Investigator: LTC Kent A. Reinker, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Surgery/Orthopedic Svc	Associate Investigators:
Key Words: Retropatellar Bone scan	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$1000. Periodic Review Results: Continue

OBJECTIVES: To determine the true nature and etiology of retropatellar pain in active duty personnel.

TECHNICAL APPROACH: Initial history will be taken to include (1) presence or absence of trauma to the kneecap; (2) presence of absence of dislocation of the kneecap, locking episodes, or effusion; (3) any recent changes in activity status; (4) presence or absence of pain on sitting or standing long periods; (5) exacerbation of symptoms with activities; (6) current activity level; and (7) duration of symptoms. Full physical examination will be accomplished to include the measurement of patellofemoral Q-angle, presence or absence of apprehension test, presence or absence of thigh atrophy, and presence or absence of subluxability of the patella. Bone scanning will be done using technetium-labeled calcium pyrophosphate. Abnormalities on x-ray or bone scan will be followed at periodic intervals. All patients with symptoms lasting three months or longer following conservative treatment will be scheduled for arthroscopic evaluation of the knee joint. Patients will be followed for six months following arthroscopy or surgical treatment if indicated.

PROGRESS: There has been inability to correlate increased technetium interface (hot bone scan) with the retropatellar pain syndrome. It is felt that retropatellar pain syndrome represents a constellation of disease. As yet, investigators have been unable to define subcategories of this syndrome.

Initial findings were presented at the Society of Military Orthopedic Surgeons Meeting in November 1979.



# Detail Summary Sheet

Date: 20 Jul 81 Prot No: 21/80 Status: Ongoing  
 TITLE: International Study on Lateral Electrical Stimulation for  
 Treatment for Scoliosis

Start Date:	Est Comp Date:
Principal Investigator:	Facility:
LTC Kent A. Reinker	Tripler Army Medical Center
Dept/Sec:	Associate Investigators:
Dept of Surgery/Orthopedic Svc	LTC Lynnford S. Wilson, MC
Key Words:	
Scoliosis	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$800.
	Periodic Review Results: Awaiting approval

OBJECTIVE: To investigate the treatment of scoliosis in adolescents using stimulation of lateral musculature.

TECHNICAL APPROACH: Juvenile and adolescent scoliosis patients with curves between 20 and 45 degrees and projected Hawaii residency of greater than two years will be offered admission to the study. Informed consent will be obtained. Standardized x-rays will be taken to document pretreatment status. Two stimulation electrodes will be placed in the lateral musculature at the apex of curvature and the muscles stimulated. Normally a 200 microsecond pulse at a rate of 25 pulses per second and 40 to 50 milliamperes, 8 volts is utilized. An x-ray will be taken documenting improvement of the curve with stimulation. After initial familiarization, stimulation is used nightly during the normal hours of sleep. Follow-up will be obtained two weeks following treatment and at three-month intervals thereafter. The electrical equipment will be calibrated at each clinic visit. Patients will be treated until full bony maturity has been obtained using standard radiographic criteria. Progression despite treatment or failure of patient compliance will also be grounds for termination of treatment.

PROGRESS: Awaiting OTSG approval.

# Detail Summary Sheet

Date: 20 Jul 81 Prot No: 30/80 Status: Ongoing  
TITLE: Upper Extremity Fractures in Children

Start Date: Sep 80	Est Comp Date: Sep 81
Principal Investigator: LTC Kent A. Reinker, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Surgery/Orthopedic Svc	Associate Investigators: CPT Edmund C. Landry, MC
Key Words: Fractures, upper extremity	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$500.
	Periodic Review Results: Continue

OBJECTIVE: To determine the results of treatment of upper extremity fractures in children at Tripler Army Medical Center with specific regard to malunion, nonunion, and other complications.

TECHNICAL APPROACH: Orthopedic outpatient files from 1970 through 1973 (last year fully available) have been searched and fractures involving the upper extremity in children from 0-15 years have been evaluated. New information has been summarized into categories of the patient's age, the length of follow-up, the diagnosis, complications occurring, if any, in the treatment for the specific injury. Eighteen hundred total cases have been collected. Injuries will be divided into those of the phalanges, metacarpals and carpals, distal forearm, proximal forearm, elbow, upper arm, shoulder, and clavicle. For each fracture site, the average age, length of follow-up, complications, and treatment will be summarized. Due to the large number of items involved, it is felt that statistical analysis with the aid of computer programming is necessary for full realization of the information available. Attempts will be made to clarify which fractures have the greatest potential for malunion, nonunion, or delayed healing. Also, the individual forms of treatment will be classified as to their adequacy or inadequacy. Precise indications for specific therapy in each group can then be formulated.

PROGRESS: Clinical material is still being gathered and collated.

# Detail Summary Sheet

Date: 29 Jul 81 Prot No: 20/79 Status: Terminated  
 TITLE: A Demonstration of the Need or Lack of Need of Passive Drainage Systems After Cholecystectomy

Start Date:	Est Comp Date:
Principal Investigator:	Facility:
MAJ Troy M. Reyna, MC	Tripler Army Medical Center
Dept/Sec:	Associate Investigators:
Dept of Surgery/General Surgery	MAJ Anna K. Chacko, MC
Key Words:	
Cholecystectomy	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$250.
	Periodic Review Results: Terminate

OBJECTIVE: To assess the usefulness of a radionuclide, TC 99<sup>m</sup> HIDA, in demonstrating, quantifying, and following subhepatic bile collections after cholechystectomy.

TECHNICAL APPROACH: The study was designed to determine the accumulation of TC 99<sup>m</sup> in the gallbladder bed and upper abdomen with and without the use of drains postcholecystectomy.

PROGRESS: No work was ever done on this project. It is therefore terminated.

# Detail Summary Sheet

Date: 28 Jul 81 Prot No: 36/78 Status: Ongoing  
 TITLE: T-Cell Antigenicity of Canine Tunica Albuginea

Start Date: Aug 78	Est Comp Date: Sep 81
Principal Investigator: MAJ Kenneth A. Rutledge, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Surgery/Urology	Associate Investigators: COL Edward M. Blight, Jr., MC
Key Words: Tunica albuginea	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$2500. Periodic Review Results: Continue

**OBJECTIVES:** To determine by specific responses the T-cell antigenicity of canine tunica albuginea.

**TECHNICAL APPROACH:** The dog tunica albuginea will be surgically obtained along with skin specimens. The tunica albuginea will be cleaned. The tunica albuginea and skin will be sutured onto mice. The response to each sutured specimen will be judged as to their generated immune response. The sutured skin specimens will serve as controls. The amount of response to each specimen will be measured and compared to skin controls.

**PROGRESS:** This study progressed to the point of transplanting canine tunica albuginea to the backs of mice and then sacrificing mice. The slides have not been looked at yet primarily due to lack of time on the part of the investigators. It is hoped that work on this project will continue in the next fiscal year.

# Detail Summary Sheet

Date: 20 Jul 81 Prot No: 33/78 Status: Terminated  
 TITLE: Characteristic Impedances and Reflection Co-efficients of Graft-Artery Anastomoses

Start Date: Jul 78	Est Comp Date:
Principal Investigator:	Facility:
COL Paul L. Shetler, MC	Tripler Army Medical Center
Dept/Sec:	Associate Investigators:
Dept of Surgery	
Key Words:	
Graft-artery anastomoses	

Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$100.	Periodic Review Results: <u>Terminate</u>
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OBJECTIVES: To measure reflection co-efficients at graft-artery anastomoses and determine the importance of characteristic impedances in causing these reflections.

TECHNICAL APPROACH: Following insertion of a graft in continuity into a divided artery, simultaneous measurements of pulsatile pressures at two points in the graft proximal to the distal anastomoses and in the artery just distal to the anastomoses are performed. Also, pulsatile flow is measured through the graft. Pressure measurements are repeated with the artery occluded distal to the anastomosis. The reflection co-efficient is derived from this data and compared to the theoretical reflection co-efficient derived from the characteristic impedances of the artery and graft.

PROGRESS: Project terminated. Techniques and monitors too insensitive to produce meaningful data.

# Detail Summary Sheet

Date: 20 Jul 81 Prot No: 11/79 Status: Ongoing  
 TITLE: Endocardial Oxygen Supply-Demand Ratio: The Reliability of  
 Clinical Approximations in Prediction of Subendocardial Ischemia

Start Date: Sep 80	Est Comp Date: Sep 81
Principal Investigator: COL Paul L. Shetler, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Surgery	Associate Investigators: Gordon H. Bryant
Key Words: Subendocardial ischemia	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$300.
	Periodic Review Results: Continue

**OBJECTIVES:** To determine clinically useful hemodynamic factors reflecting acute subendocardial ischemia resulting from anemia-induced hypoxia.

**TECHNICAL APPROACH:** Experimental animals will be progressively exsanguinated while blood volume is replaced with dextran until a left ventricular endocardial electrode indicates ischemic changes. The endocardial viability ratio and modifications by oxygen delivery, arterial oxygen content, cardiac index, and left ventricular stroke work will be correlated with ratio of diastolic coronary blood flow and tension time index to assess the reliability of the hemodynamic factors in warning of impending subendocardial ischemia.

**PROGRESS:** Project must be simplified as production of monitor has been discontinued. It will be completed in simplified form during 1981.

# Detail Summary Sheet

Date: 29 Jul 81 Prot No: 10/77 Status: Terminated  
 TITLE: Evaluation of the Immunologic Basis for Post-renal Transplant Hypertension

Start Date: Jan 77	Est Comp Date:
Principal Investigator: LTC Douglas W. Soderdahl, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Surgery/Urology	Associate Investigators: LTC Edward Raleigh
Key Words: Post-renal transplant hypertension	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$2000. Periodic Review Results: Terminate

OBJECTIVES: To study the renal arteries of dogs that have undergone transplantation and have developed hypertension that is not responsive to the usual therapy for immunologic rejection. Arteries will be studied via angiography and microscopy to determine what role the animal's immunologic response has played in the development of fixed hypertension.

TECHNICAL APPROACH: Dogs will undergo renal transplantation after unilateral nephrectomy. Immunosuppressive therapy will be given consisting of Imuran, 10 mg/kg for 2 days, 5 mg/kg for 4 days, and 2.5 mg/kg daily thereafter. Prednisone will be given in a dose of 30 mg daily. Drugs will be given orally. Blood pressure will be monitored on a daily basis and renal function, via BUN and creatinine, on an every-other-day basis. WBC will also be obtained to avoid excessive bone marrow suppression. Clinical or laboratory evidence of rejection will be treated by an increase of the steroid dose to 100 mg/day. Should hypertension develop, the first therapy will be as if rejection is occurring. Thus, prednisone will be increased to 100 mg/day. If renal function shows no further deterioration and hypertension persists, a transplant renal arteriogram will be performed to evaluate the presence of lesions of the major vessels. Should these be present, the graft will be removed, the vasculature and parenchyma will be studied with routine microscopy, and immunofluorescent studies for the immunoglobulins, complement, fibrinogen, and albumin will be performed on the vessels.

PROGRESS: This study has been terminated due to lack of technical ability to stain the renal arteries for immunologic reactivity.

# Detail Summary Sheet

Date: 21 Jul 81 Prot No: 2/80 Status: Completed  
 TITLE: Prediction of Fertility after Varicocele Correction by the  
 Zona-Free Hanster Ova Technique

Start Date:	Est Comp Date:
Principal Investigator:	Facility:
COL Douglas W. Soderdahl, MC	Tripler Army Medical Center
Dept/Sec:	Associate Investigators:
Dept of Surgery/Urology	CPT George G. Mygatt, MC
Key Words:	
Varicocele	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$1500. Periodic Review Results:

**OBJECTIVE:** At the present time no prediction of human male fertility exists in a laboratory model. The hamster zona-free egg has promise as an in vitro test system for human fertility. It is planned to make use of this model to predict the fertility of human males after varicocele surgery.

**TECHNICAL APPROACH:** Varicocele surgery was performed in 20 men with infertility and varicoceles. Spermatic activation of hamster zona-free eggs was performed before, three, and 24 months after surgery. The number of impregnations by these men for the one year previous and the one year following surgery was determined. A regression analysis of the results of the in vitro prediction of fertility with the actual fertility of the men before and after surgery was analyzed. The hamster zona-free egg analysis was performed by Dr. B. Jane Rogers of the University of Hawaii.

**PROGRESS:** The hamster egg fertilization assay is a more sensitive index of fertilization potential of sperm than other current tests. No one who began with a fertilization rate of 0% was rendered fertile by surgery, perhaps allowing us to be more selective in the future in deciding who should have an operation. Improved fertility after high ligation is paralleled by an improvement in fertilization rate. It is interesting to speculate that someday we may be justified in performing high ligation in infertile men with varicoceles, whose only semen abnormality is a decreased fertilization rate.

The study results were presented orally at the Kimbrough Urologic Seminar, San Diego, California in 1980, and Dr. Mygatt, co-author with Dr. Soderdahl, won Second Prize for the best resident paper. Dr. Soderdahl plans to present this at the annual meeting of The American Urological Association in May in Boston. A written paper is contemplated.



# Detail Summary Sheet

Date: 20 Jul 81 Prot No: 17/80 Status: Terminated  
 TITLE: Piriformis Syndrome

Start Date:	Est Comp Date:
Principal Investigator:	Facility:
COL Dennis J. Sullivan, MC	Tripler Army Medical Center
Dept/Sec:	Associate Investigators:
Dept of Surgery/Orthopedic Svc	CPT Rhett K. Rainey
Key Words:	
Piriformis syndrome	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$200.
	Periodic Review Results: Terminate

OBJECTIVE: Clinical review of back and buttock pain attributable to the "piriformis syndrome."

TECHNICAL APPROACH: A retrospective record study of patients treated with this diagnosis as outpatients will be conducted on the Orthopedic Surgery and Physical Medicine Services in order to characterize clinical findings necessary to make the diagnosis and the response to specific therapy. In addition, follow-up through reexamination will be conducted when possible.

PROGRESS: This study has been terminated because clinical material was unavailable.

# Detail Summary Sheet

Date: 4 Aug 81 Prot No: 22/77 Status: Ongoing  
TITLE: Teflon Injection Indications

Start Date:	Est Comp Date:
Principal Investigator: COL Thomas E. Van Sant, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Surgery/Otolaryngology	Associate Investigators: LTC Donald W.S. Yim, MC
Key Words: Teflon Injection	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$200.
	Periodic Review Results: Continue

OBJECTIVES: To participate in expanded clinical trials of Ethicon Polytef Paste for Injection for the following clinical indications: the selected treatment of patients with velopharyngeal insufficiency and/or abnormally patent eustacian tubes.

TECHNICAL APPROACH: The protocol will follow the clinical study group proposals. Patients will originate in the ENT Clinic. Only patients who have not responded to conventional treatment modalities will be considered. The procedure with its possible risks will be explained to the patient, as well as its investigative nature. If the patient agrees to participate, the case history will be forwarded for consideration to the study group who will furnish the necessary material (Teflon). Patients will require hospitalization for approximately 1-3 days for the surgical procedure which will be done under appropriate anesthesia. Surgery time will be 30 minutes to one hour. The patients will continue to be followed on an outpatient basis for a minimum of 90 days as required by the protocol.

PROGRESS: This protocol was developed to permit utilization of Teflon injection techniques as treatment for the listed indications. The medical conditions listed occur very infrequently to the degree that this alternative therapy is required. Consequently no patients were entered into this protocol during this past year. However, the protocol will be kept ongoing should the indications for treatment occur.

# Detail Summary Sheet

Date: 20 Jul 81	Prot No: 10/80	Status: Completed
TITLE: Comparison of Ureteral Plication Technique with Standard Tailoring Technique in Treatment of Megaureter		
Start Date: Mar 81	Est Comp Date:	
Principal Investigator: CPT Shaw P. Wan, MC	Facility: Tripler Army Medical Center	
Dept/Sec: Dept of Surgery/Urology	Associate Investigators: LTC Michael Uechi, MC	
Key Words: Megaureter Ureteral plication		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$2000.	Periodic Review Results:

**OBJECTIVES:** To compare the ureteral plication technique to the standard form of treating megaureter.

**TECHNICAL APPROACH:** Ten mongrel dogs, male and female, weighing between 30 and 60 pounds, were used. In phase one of the study, the ureteral dilatation was created by ligating the left ureter at the ureteral vesical junction with a single 2-0 silk tie through an inferior laparotomy incision. The right ureter was not disturbed. In phase two, operations were carried out to correct the obstructed and dilated ureters six to nine weeks after their ligation. The dogs were divided into two groups at the second operation. In group one, comprising four dogs, ureteral plication was performed as described by Starr. The ureters were divided just proximal to the obstructing ligature, and the inferior half of each ureter was freed from the posterior peritoneum by gentle dissection. The ureters were then plicated over a 10 Fr. or 12 Fr. red Robinson catheter, depending on the size of the ureter. Plication was performed by placing inverted Lembert stitches of 4-0/5-0 chromic catgut through the lateral wall of the ureter to plicate the redundant ureteral tissue snugly over the catheter. The Lembert stitches were set 1 cm apart and were reinforced with simple 4-0/5-0 chromic catgut sutures in between. The ureters were reimplanted into the bladder using the Politano-Leadbetter technique. In group two, the control group with five dogs, the obstructed ureters were simply divided above the ligating suture, the lower one-half freed, and reimplanted into the bladder with the same technique. There was no attempt to tailor the ureters. Postoperative results were assessed by direct inspection at 8 to 10 weeks.

PROGRESS: It has been shown that the ureter has the inherent ability to correct dilatation resulting from an acute obstruction if the obstruction is relieved within a certain time. Judging from our controls, this is apparently true in dogs, at least up to 6 to 9 weeks after the ureter is blocked. In our experiment the dog ureters were ligated with 2-0 silk ligature, whereas Starr used 1.5 cm aluminum bands. In reviewing the reference Starr cited for using the aluminum band, we do not feel that the difference in the material used to obstruct the ureters would cause a difference in results. Starr has devised a simple and psychologically sound procedure to correct the massively dilated ureter. However, the animal model in his experiment is faulted by the inherent ability of dog ureter to improve spontaneously within the time used. A different experimental model is needed to further test the ureteral plication technique.

Submitted to Journal of Investigative Urology.

# Detail Summary Sheet

Date: 20 Jul 81      Prot No: 13/80      Status: Ongoing  
 TITLE: Ureterogastric Urinary Conduit

Start Date: May 80	Est Comp Date: May 82
Principal Investigator: Cpt Shaw P. Wan, MC	Facility: Tripler Army Medical Center
Dept/Sec: Dept of Surgery/Urology	Associate Investigators: COL Edward M. Blight, Jr., MC COL Peter J. Barcia, MC
Key Words: Ureterogastric urinary conduit	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$1500.
	Periodic Review Results: Continue

**OBJECTIVE:** To investigate the feasibility of using gastric antrum as an alternative conduit for urinary diversion and as a substitute for the urinary bladder. To compare the advantages/disadvantages of gastric conduit to the present methods of urinary diversion.

**TECHNICAL APPROACH:** The technical approach of this project is through a standard midline laparotomy incision. A gastric pouch is created from the greater curvature of the stomach with vascular pedicle from the left gastroepiploic artery. The ureter is then diverted into the gastric pouch and the gastric pouch is brought to the skin as a cutaneous gastrostomy. Preoperative and postoperative renal function is assessed. In addition, electrolytes and gastrin are assessed.

**PROGRESS:** Five dogs have undergone ureterogastric urinary conduit operations. The results were good, showing that the gastric pouch can be used satisfactorily as a urinary diversion conduit. Further study is needed to assess whether there is advantage of gastric urinary conduit over the standard colonic urinary conduit. Five additional dogs are needed to complete this project.

# Detail Summary Sheet

Date: 30 Jul 81 Prot No: 21/78 Status: Ongoing  
 TITLE: Strain Differences of Staphylococcus aureus Based on Lipid Analysis

Start Date: Mar 78	Est Comp Date: Sep 82
Principal Investigator: LTC David K. Ohashi, MSC	Facility: Tripler Army Medical Center
Dept/Sec: Health Services Command	Associate Investigators: CPT Carroll R. Dotson, MSC
Key Words: <u>Staphylococcus aureus</u>	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost: \$1500. Periodic Review Results: Continue

OBJECTIVE: To examine the feasibility of determining strain differences of Staphylococcus aureus by analysis of gas liquid chromatography (GLC) fatty acid profiles. If strain differences can be demonstrated, epidemiologic analysis can be simplified, and rapid laboratory analysis can be made without resorting to time-consuming phage typing.

TECHNICAL APPROACH: Strains of S. aureus will be collected and identified to species by the Microbiology Section, Department of Pathology, TAMC. Organisms will be prepared for gas chromatographic analysis using a modification of the method of Ohashi. Briefly, whole cells will be prepared for GLC analysis using tetramethylammonium hydroxide by a very simple procedure requiring less than two hours for the preparation of a dozen samples. The organisms will grow on several media formulations to determine which media will enhance lipid accumulation by the strains being examined. Gas chromatographic data will be subjected to pattern analysis and strain differences will be defined in terms of observed variations.

PROGRESS: Because of higher priority being given other work, further progress in the laboratory has not been accomplished. However, a means by which oxidation of materials can be prevented has been devised, and manipulation of cell lipid composition is planned.

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